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RANDOM REMINISCENCES OF LAST CENTURY EUROPEAN OPHTHALMOLOGISTS

ALEXANDER W. STIRLING, M.D.

BALDWIN, GA.

My earliest association with ophthalmology was at the Sunday morning operations at the eye clinics in the Royal Infirmary in Edinburgh in 1879 and 1880, my last two years at the University of Edinburgh. There were then two surgeons attached to the ophthalmic wards. Mr. Walker, unknown to fame, was big, inelegant, good natured and short sighted. He appeared even to novices like myself to do what not a few novices unwillingly accomplish in another field of endeavor; that is, he demonstrated perhaps to a critical audience how to do everything one wishes to avoid when striving to make a clean job, keep on the fairway and plump into that elusive little hole by the shortest route possible. Yet the house surgeons stated that his results from the point of view of the patient were as good as those of his famous colleague Mr. Argyll Robertson.

In parenthesis here I may explain that students in Great Britain do not graduate into the title of doctor of medicine. This is a higher degree. It may be obtained by the ambitious not before two years of postgraduate practical work and is no aspiration of the pure surgeon, who distinguishes himself by remaining simple "Mister," with the title of bachelor of medicine from a university or a diploma from one of the colleges. Though all general practitioners are called "Doctor" by their patients and friends, many—perhaps most—of them have no official right to the title. Applicants for appointments in the hospitals of the larger cities are expected to have taken the fellowship of the Royal College of Surgeons, which means that they have passed exceedingly searching ordeals in anatomy, physiology and surgery, even if they have no intention of practicing general surgery. These examinations are intended to weed out the mediocre in ability and character. Members of the medical profession never call one another "Doctor" in Britain without adding the surname.

This paper was read before the Ophthalmological Section of the Atlanta Academy of Medicine on June 13, 1927. I was asked to publish it at the time, but it was laid aside and forgotten. I came across it recently, and on looking through it I thought it might still interest students of eye work and its history.

Mr. Argyll Robertson was a striking figure, especially when rigged out in the arresting uniform of the ancient company the King's Body-guard of Royal Archers, a relic of the days when a Scottish sovereign prohibited all such unmartial games as football because they wasted time which should be given to attaining proficiency in planting arrows in the eyes or between the ribs of encroaching Englishmen. It is related of a cousin of mine that she paid her 2 guineas not so much that Argyll Robertson might examine her eyes as that she might gaze into his. It is not always mere cold ability that makes the successful physician. It was said to be because he was not altogether unaware of his natural attractions that, though subject to the common assaults of time, he refused the aid of the glasses he seemed content to prescribe for other persons. Those were the days of general anesthesia and in Scotland of chloroform at that. Scots were supposed to be almost immune to a dose of chloroform that would perish a mere Englishman. Perhaps this was on account of the supposed resemblance between its chemical formula and that of the national beverage. I distinctly recall an unhappy result of the combination of indifferent anesthesia and Argyll Robertson's uncorrected presbyopia. During an extraction he failed to observe that his Graefe knife had penetrated the iris. The patient, however, did not, and he responded with such an energetic spasm of the lids that the lens sprang a foot in the air and landed on the instrument table. My first ophthalmoscope was his invention. I sent it years ago to a show of ancient instruments in Chicago. Somebody must have fancied it for his wife's vanity case, for it never came back to me. It was a little flat black wooden box with the eye hole in the bottom. On removing the lid one discovered the object lens and saw that the bottom inside was composed of a perforated concave mirror. Argyll Robertson, so far as I can remember, used only the indirect method. His name is linked with fame because he was an acute observer and his pupil was a step forward in neurology. At length he exchanged the cold winds of the "gray capital of the North" for the warmth and color of the palace of a friend of his, one of the great Indian maharajahs, and there he died.

Speaking of those far away days in Edinburgh reminds me of Arthur Conan Doyle and that he was once an eye specialist. My acquaintance with him was confined to sitting near him in Turner's class on anatomy; to looking with him in wonder at Mr. Joseph Bell, the prototype of Sherlock Holmes, as he told us a great deal about the patients before they had mentioned their symptoms; to receiving a not too grateful letter from him when I ventured, entirely for the sake of his good name, to point out as courteously as possible that in one of his books there was an error, no doubt a printer's error, whereby the convexity and concavity of a pair of spectacles had obviously got mixed, and to telling him that in a copy of another of his books, borrowed

from the Carnegie Library. some one had scribbled on the margins of the leaves most uncomplimentary objections to himself. These objections, I may say, were not altogether unjustified, since he had introduced a case of miscegenation between a white person and a Negro as apparently legal instead of criminal in Georgia.

When I attended the clinics of Berlin there were three professors of ophthalmology who, I understood, were paid by the state. Schweigger, Schoeler and Hirschberg.

Schweigger, I believe, was the immediate predecessor of the senior Knapp of New York and was summoned from New York to a chair



Fig. 1.—Douglas Argyll Robertson (1837-1903).

in Berlin University. I did not greatly admire Schweigger. I do not consider slashing operations in place in the eye, and he struck me as the slashingest eye surgeon I had ever seen. He extracted cataracts while sitting on the edge of the ward bed with his legs under the patient's arm. The lids were held open by an assistant with a pair of retractors. He used a blunt prong in place of a fixation forceps, a triangular Beer knife, and he cut upward and away from himself coming out 3 or 4 mm. from the cornea. I saw him once nearly open the ciliary region while the vitreous came through with a rush. He did no iridectomy.

Schoeler, on the other hand, was a careful operator. He also worked from the front of the patient and cut away from himself. He extracted the two lenses at one time if they were "ready." His patients walked to and from the operating table, upstairs and downstairs and sometimes to the far end of a long rambling building. No harm, he said, resulted. I saw Schoeler, in order to prevent sympathetic involvement, do the following operation on a woman entirely unanesthetized: He fixed the external rectus muscle on a thread, divided the muscle, cut the optic nerve, drew the stump around to the front, cleared the back of the eye and replaced it.

I was sorry that Hirschberg at the time was in India, because I was told that he was the best ophthalmologist of the three. He was of Jewish extraction and was held in high esteem.

I spent only three months in Berlin, but they were rather strenuous, for there was no lack of material and at the same time I was studying with care Fuchs's famous book. The Germans had managed at that time to convince the youth of the world that science began and ended with them. But so far as work on the eye was concerned I, for one, failed to be deeply impressed with Berlin. Examinations seemed to be far from thorough and the results nothing to boast about. With the ophthalmoscope the Germans claimed commonly to be able to distinguish the most minute changes even close to the macula without the aid of a mydriatic. After my return to London I asked Nettleship, certainly one of the most able and reliable of ophthalmoscopists, what he thought of that. To disprove the reliability of such examinations he quoted an experience of his own. He had succeeded a typical German surgeon as ophthalmologist at St. Thomas' Hospital and thus had fallen heir to his patients as well as to his notes. He said that his own examinations of the fundus, a mydriatic being used, revealed a constant stream of pathologic changes which had been missed. Nettleship's book on diseases of the eye ranked high in those days, as he did himself among the senior ophthalmologists. He was specially interested in the question of heredity. For example, he made a study of its relation to retinitis pigmentosa. He found that in 23 per cent of cases he could trace heredity without consanguinity, in an equal percentage consanguinity without heredity and in 3 or 4 per cent heredity combined with consanguinity. One third of the patients were deaf, and others showed cerebral or other defects.

In those days there was nowhere such minute and careful attention to asepsis as is now universal. In Germany asepsis was more apparent in theory than in practice. I find that frequently in my notes I speak of Silex with much respect, as one of the younger men who promised to make a name for themselves. Silex was conducting Hirschberg's clinic in his absence. I also find many references in

my notes to Dr. Perles. Albrecht was Schoeler's assistant. All things considered, I came to the conclusion that the common opinion of the time in America and Britain concerning the relation between surgeon and hospital patient in Germany was justified—the Lord had provided the superior being with common clay on which to work out his theories and incidentally to learn his business. The casual manner of the one toward the other I saw exemplified one morning when I looked in on Hartmann's clinic. Hartmann and his book on the ear were then famous. He was a magnificent physical specimen, but I thought him a little careless of common humanity when he had a patient



Fig. 2.—Dr. Joseph Bell.

stretched out on one of the waiting room forms while he operated on his mastoid with hammer and chisel.

I do not remember where I got the following information, but I think it was from Schoeler himself. Of the three professors paid by the state Schweigger got the patients who could not pay. The fees at Schoeler's clinic were: first class, 10 marks; second class, 7½ marks; third class, 4 marks; fourth class, 2½ marks. Patients also paid for drugs, and they paid up to 6 or 7 marks for visits as well as varying amounts for operations. Removal of a cataract might cost as much as 600 marks. But Schoeler paid the "inspector," his assistants and the porter. The house belonged to him. He supported thirty people.

I had been undecided whether to go to Berlin or to Vienna. From friends who had been to Vienna I had gathered that excellent tutorial classes for students had been arranged there with a special eye to American beginners, while I had already been working in ophthalmology for some years. I fancy that there was another reason for the popularity of Vienna. It was a gay and merry city, and there was not that undercurrent of jealousy of Britain and America which was already in process of development in Berlin. Besides myself there was only one English-speaking student in Berlin who was working on the eye: Rowan, who now, I understand, is doing well in Glasgow.

Now my notes take me to London. As in Berlin, I made one of nearly every interesting case I saw. I can cull only a handful to illustrate important debates of days gone by.

In London as elsewhere the debate on iridectomy in the extraction of cataracts went on apace. Shall one snip a piece off before removing the lens? If so, how much and where? "Snip" said they of the school of safety first. But "No," replied their opponents with a vigor equal if more restrained, "we'll take the risk because there need be no prolapse, while the patient will look better to us and we'll look better to him." One surgeon, determined that there should be no prolapse in his cases, removed as much iris as he could coax within the teeth of his forceps. He was Mr. Couper, the inventor of a refracting ophthalmoscope 8 or 9 inches (20 or 23 cm.) long, afterward improved by Mr. Morton's chain of lenses. At his house Morton taught classes of three at a time how to operate on the eyes of pigs, including the lids. He was himself a most dextrous operator, and he wrote an excellent little book on refraction. Before his extractions he instilled physostigmine salicylate solution in order to deepen the anterior chamber and permit of a delicate grip on the pupillary margin of the iris. The instillation of this solution also tended to prevent postoperative prolapse of the iris. He removed the smallest amount possible at iridectomy, his desire being merely to get rid of the tension of the ring muscle. The theory then commonly held at Moorfields (Royal London Ophthalmic Hospital) was that the resistance of this muscle to the escape of aqueous was the cause of prolapse. Morton therefore cut the iris with scissors pointed not across but toward himself. He pulled out the iris with a Tyrrel hook. When he died he left his ophthalmoscope as a monument to his name.

The majority of the London ophthalmologists favored iridectomy. William Lang—it was he who first directed attention to the relation between diseased teeth and certain ocular infections—was in London the most influential advocate of simple extraction. But after the lens was out he made a point of replacing the iris with forceps. His hands

were small, lady-like and shaky, but I know no man I should have preferred had I been in the unfortunate position of needing an eye operation, because he always shook into precisely the right position. I look on Mr. Lang as having ranked among the best of modern ophthalmologists and the most stimulating of teachers.¹

A hole² in the iris close to its external periphery, made after the extraction, long popular in Britain, appears to me most satisfactorily to settle the question of iridectomy, because it permits the free passage forward of the aqueous, is invisible and leaves a normal round pupil.

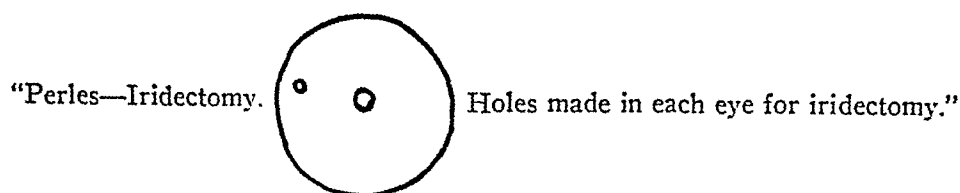
The proper treatment of the lens capsule was then another subject of debate in London, because Mr. Couper was advising, and himself practicing, the removal of the anterior layer with a special six-toothed forceps. He opened the forceps widely before closing it and gently shook it, and away came the membrane. This maneuver produced a fine clear pupil, which remained so for a while. But it found few disciples, mainly because the posterior layer remained and on it there was likely to develop a deposit of proliferating cells, while even a crinkling of its surface is enough to interfere with vision and necessitate a needling.

It used to be said at Moorfields that needling caused a number of infections entirely disproportionate to the severity of the operation. That may have been because then it was too lightly considered and too carelessly performed. It is now known that, as Mr. Lang pointed out to his students, the needle should be of exactly the same diameter throughout and perfectly round, should be introduced under the conjunctiva and should be withdrawn with the utmost care because, as Mr. Treacher Collins showed, glaucoma has been caused by the dragging of a scrap of capsule into the corneal wound.

There was then considerable difference of opinion over the treatment of juvenile soft cataracts after they had been needled. One side said "Leave them alone to be absorbed." The other advised their immediate removal by suction through a small flat cannula attached to

1. When "Willy" Lang died the medical profession lost a most endearing character. His son, who promised to fill his shoes, died soon after him.

2. April 1941—On glancing over my notes made in Berlin in December 1892 I notice the following which I quote exactly as then written:



a tube, the motive power being supplied through the tube either by the mouth of the operator, some fluid intervening, or by a delicate syringe. The results after suction were brilliant, and the risk of secondary iritis was diminished. But as the eye was opened there was the risk of infection. One or two of the surgeons used a somewhat similar simple apparatus to wash out the debris remaining after extraction of a senile cataract, but it was generally preferred to coax it out through the cornea.

Mr. Hartridge, one of the senior surgeons to the Royal Westminster Ophthalmic Hospital, at Charing Cross, had written the most popular book on refraction. Of a charming personality, he was an excellent teacher of his special subject and also a fine diagnostician. I did not, however, rank him, or indeed any other of the surgeons to this hospital (where I was for long a clinical assistant and later house surgeon), as a topnotch operator. They were therefore all the more amenable to any gentle hint that the house surgeon had no insuperable objection to taking their place. I thought them very gentlemanly in that respect. One of their most valuable enterprises was the monthly clinical evening, arranged by each surgeon in turn. He was expected to beg, borrow or steal every good case of an abnormal fundus that he could lay his hands on. There were met many famous surgeons from elsewhere. A slip of paper detailing the fundus picture was laid face down beside the case report, and one was expected to make a diagnosis before looking at it.

Priestly Smith, of Birmingham, was a particular friend of Mr. Frost, the senior surgeon, and came to the hospital occasionally. It will be recalled that his experiments on ocular tension and his book on glaucoma made a profound impression. He had been an engineer before studying medicine and was therefore well prepared for his delicate experiments, which led to the conclusion that the immediate causes of the high tension were mechanical. High tension he found was most likely to appear when the cornea was small, indicating that the space between lens and ciliary body was unduly narrow, the anterior chamber shallow and the exit of the ocular fluid easily blocked at the angle.

His atlas of the fundus was Frost's chief claim to fame. The pictures used to be thrown on a magic lantern screen while he pointed out what was particularly interesting. He retired comparatively young to wander over the face of the earth. He said that he had once invited Fuchs to stay the night with him. Fuchs shook his head and took a shot at the British proclivity for enucleation. "No, thank you," he said. "I fear that when I waked I should have but one eye."

The fear of sympathetic involvement was something of a nightmare wherever there turned up a doubtful wound of the eye. The risks taken on the continent were considered unjustifiable in Britain. The causation was constantly debated and never settled.

In order to mitigate the unpleasing effects of enucleation or simple exenteration, Mules, of Manchester, introduced his operation of clearing out the contents of the sclera and inserting a glass ball. This was received with mixed feelings, for many surgeons feared sympathetic involvement. The results at the time were beautiful to behold, and I did half a dozen of the operations. But the operation as then performed was doomed to ultimate disfavor. Often the ball was discharged because it was too big; it might be smashed, and if I am not mistaken there was a case or two of sympathetic involvement. Still the operation was the initial step in a movement that has been of benefit to persons who for their own sake and that of others care for their appearance, one of the commonest of virtues. Frost replaced the glass by lumps of fat, which soon disappeared. Webster Fox used gold balls, all manner of replacements were tried and now simple enucleation has gone out of fashion.

In those days there was considerable difference of opinion concerning the treatment of conical cornea. Some surgeons removed a wedge from the apex with a Graefe knife, but the best instrument seemed to be the cautery. It was said that the size of the wound should be proportionate to that of the cone, but at least 3.5 to 4 mm. in diameter; that the edges should be vertical, and that it should reach Descemet's membrane. Debate again arose: To perforate or not to perforate? As opinion appeared about equally divided, some authorities decided to compromise and merely pop the cautery through the center of the wound. It was of course deemed of great importance that the patient lie flat on his back until the wound had thoroughly healed. Can surgeons do any better now?

In my old notes I find frequent reference to names I have not included in these very random reminiscences. Among the most notable of these are Mr. Marcus Gunn and Sir John Tweedie.

Among his colleagues modest, gentle, Mr. Gunn was recognized as a supremely reliable observer and interpreter of the most minute details of intraocular disease. His name will go down to posterity through "Gunn's dots." These, as is well known, are best seen with a dim light. They are found near the disk in healthy dark persons who complain of dazzling in a bright light. They seem to run in families. Mr. Gunn believed them to be large ganglion cells or groups of cells. His custom in refraction was to measure with the direct method applied to arteries at right angles. He did preliminary iridectomy in the treatment of cataract.

Sir John Tweedie, with quite a grand presence, was something of a scholar, gave the impression of being rather lazy and used to entertain his audience in the operating room with reminiscences surgical and otherwise. He wrote little, which is to be regretted, for out of

his vast experience he could have made a valuable book. I recall his dictum that the word *nictalopia* is properly employed to mean night blindness and not day blindness, as is the case in at least some parts of the Continent. He was greatly admired by his confrères and was elected president of the Royal College of Surgeons.

In those days the bright particular stars in the ophthalmic firmament of France were Landolt, who was a Swiss; Wecker, whose name at least suggests a German or border heritage; Galezowski, a Pole; Panas, a Greek, and Trousseau, who, I suppose, was pure French. Trousseau was perhaps the first to eliminate both speculum and cystotome in extractions of cataracts. He held the lids open with his fingers and sliced the anterior layer of the capsule with his knife as it crossed the pupil.

Landolt was a good-looking and agreeable person and spoke excellent English. I remember him most clearly when pulling black hairs out of my eyebrows, because he said that raven hairs had no business among the gold. He had invented a rather complicated toy, called Landolt's ball, for the purpose of simplifying his explanation of the ocular movements.

Wecker seemed to me the most striking of the Parisian ophthalmologists. As I recall him he was a big, heavy, brusque person with a large bald head. He had some abnormality of vision, I think high myopia with divergence; at any rate, when he operated his nose nearly touched his patient's. Wecker was the great exponent of the theory that it is through the formation of a filtering scar that operation cures glaucoma. He experimented with sclerotomy alone but returned to a combination with iridectomy. Elliot's trephine hole is simply the realization of older attempts to make a scar that would filter. Collins showed that the scar, because of the watch glass insertion of the cornea, was generally in the cornea at least as much as in the sclera and was rarely any more pervious than the original tissue. Colonel Herbert, after immense experience as an ophthalmologist in India, actually recommended and practiced in the treatment of noncongestive and moderately congestive glaucoma a wide subconjunctival incarceration of the iris in the wound for the sake of diffused drainage. Wecker himself used to be rather pleased to have an inclusion of the iris for the same reason. Herbert expressed the belief that his operation is absolutely safe in every way except for the risk, common to all operations for glaucoma, of endogenous uveitis and secondary cataract. I doubt his converting many of the skeptics, any more than Wecker did.

Glaucoma has afforded the widest field in ocular pathology for the scintillation of the surgeon's imagination, and I would say to any inquiring young and ambitious ophthalmologist "If you really wish to know the eye, study the history of glaucoma."

I recall especially two dogmatic assertions of Wecker's: that there is no such thing as tobacco amblyopia and that the defective vision thought to be due to the use of tobacco is always due mainly to the use of alcohol. He declared that to give up only tobacco will not improve the vision while stopping the use of alcohol and continuing to use tobacco will. He cited in support of his statements conditions in Paris during the siege of 1870, when there was much drunkenness and little food, and mentioned the Cubans, who are the heaviest smokers on earth and never suffer from tobacco amblyopia unless they drink. Back in London, I put the question to Nettleship. He said he had looked up his notes on private patients with tobacco amblyopia and had found that 8 were teetotallers, that 1 was a woman who drank heavily but was not known to smoke and that another was a publican, or saloon keeper, who smoked only one cigar or so a week and improved on stopping the use of alcohol. A little later Berry, of Edinburgh, told me he had seen 30 teetotallers with tobacco amblyopia. This divergence of opinion was explained by the difference in the tobacco and in the alcohol of France and of Britain.

Wecker in his vehement way differed from his London colleagues on the question of the removal of wounded eyes as a precaution against sympathetic involvement. I saw eyes retained in his clinic and in Landolt's that would have been immediately excised in England. Wecker affirmed that because only 5 per cent of wounds of the ciliary region ever caused sympathetic involvement it was foolish to remove every possible exciter, especially if the conjunctivas were sewn over the wound.

At this time Wecker was already operating for detached retina by cauterizing once a week for perhaps ten weeks over the site of the detachment. He penetrated the sclera but tried to avoid going entirely through it. His good results he attributed to resulting choroiditis with adhesions.

I recall a scene in Wecker's clinic which illustrates the attitude of Continental surgeons toward their charity patients. A young man under whose conjunctiva Wecker was preparing to inject a solution of mercury bichloride, suddenly experienced a change of heart, or felt that his feet had gone into cold storage, or acted on some other motor impulse. He leaped from the table and made for the door. *Mon dieu! Sacré! Mille tonnerres!* The whole staff was after him, surgeons, students, aides. They seized him by the hair, the arms, the legs; they carried him kicking and fighting to the table and held him there while the triumphant surgeon stuck the needle in his eye.

Dr. Bull, of Montreal, trained in the Manhattan Eye, Ear and Throat Hospital, carried on a large practice chiefly in refractions among both English-speaking people and the French. He later read before the British Ophthalmological Society a paper on the *clignement* or pressure

of the lids as affecting the shape of the cornea. It was favorably criticized at the time, and Parsons in the 1927 edition of his book said: ". . . the radius of curvature of the horizontal meridian (of the cornea) is longer than that of the vertical. Perhaps the pressure of the lids on the globe tends to squeeze it above and below." But I believe I rather conclusively proved in papers published in 1920 and 1921 in the *ARCHIVES* and elsewhere that the axis of astigmatism generally swings with the years and almost always in a direction opposed to that indicated by Bull's theory. Bull was good enough to invite me to become his partner, but to do so would have meant passing a searching examination in the very rudiments of medicine, and that in the French language; so in spite of the fact that Paris was such a delightful city that all good Americans went there when they died, I declined the honor with many thanks.

Some one took me to see Javal, to whom so many ophthalmologists in this country seem to think they owe a debt of gratitude. I was told that the mathematics of the Schiötz-Javal instrument were worked out chiefly by Schiötz, a Swede. Javal was a sad picture, growing gradually blind, I think from glaucoma. Yet he remained cheerful and agreeable. No ophthalmometer ever found much favor with British ophthalmologists. For refractive purposes they gave their heart to retinoscopy, the child of their own Sir William Bowman. But some of them, like Hart-ridge and Gunn, were averse even to retinoscopy for students. They advocated making the preliminary measurements of refraction by the direct method because to do so provides the most thorough training. This I will say: I believe Javal's and every other ophthalmometer have been by no means a blessing to American ophthalmology and should be abolished in every clinic.

My personal feelings toward Galezowski are mixed. I remember him as a large rotund man who had married a celebrated countess and had invented a prismatic ophthalmoscope with the object of bringing into view the more anterior area of the fundus and as inviting me to dinner. That dinner makes me creep inside. I never ate it. It was set for 7 o'clock at his house. At 7 o'clock or after in my room in the famous Boul' Mich', the stout form of Dr. Galezowski, up to that moment crowded out of mind by his own and other interesting cases, again dawned on my consciousness and nearly swept it out of existence. I don't know what I said in the letter I concocted while waiting for the messenger, but as in those days I had a notion that honesty was the best policy it was probably a frank and humble confession of sin. Galezowski unwittingly had an ample revenge for my rudeness. The shah of Persia, the king of kings, had an eldest son, Zille Sultan, the shadow of the king. That shadow was afflicted in the eyes. The shah cabled Galezowski to come posthaste to Isfahan or to send some one in his stead.

Galezowski hit on Treacher Collins as his substitute. Collins had been for some ten years pathologist to Moorfields and was thinking of resigning. He was also thinking about a certain young woman from New Zealand and a honeymoon when Galezowski's message so timeously arrived. What a happy coincidence! A trip with his bride to Ceylon and thence up the Persian Gulf to the palace of the king of kings! Did *Collins* forget Galezowski's invitation? Oh, no! And here is how my humble life was affected. I had been working with Collins two or three times a week for a year in the Moorfields laboratory, and he had suggested that I might be a suitable person, not of course to fill his shoes, but to step into them. Along with other work, I had searched the pathologists' notes made during thirty years for cases of primary sarcoma of the orbit. I had found and examined the notes on 29 cases. I had also examined the vortex veins of twenty eyes enucleated for primary glaucoma. Full details on these were published in the *Royal London Ophthalmic Hospital Reports* for 1893.

As fate would have it, a few days before the arrival of the shah's cable I had decided to visit friends and the clinic in Edinburgh and departed without saying where I was going. When I arrived back at Moorfields a fortnight later Collins and his wife were already well on their way to Persia and a nice chap called Marshall was comfortably installed in the laboratory. He became full surgeon in due time. That's what Galezowski and the king of kings did to me.

On his return Collins wrote an interesting book with the title "In the Kingdom of the Shah." As "the great hakim" he had such crowds of patients that it was found necessary to call out the military to keep them at a distance. He told me that extracting cataracts was "just like shelling peas." The wild Bakhtiyari from the adjoining mountains were specially grateful. Among their offerings were Arab steeds, but such matters as carpets were more portable. It was a splendid experience, but unfortunately it was considerably spoiled on the way home, both for him and for Mrs. Collins. He had maintained a delusion, shared I understand by his brother, Sir Joseph, that vaccination was valueless against smallpox, and he had skipped the little operation. He had ample opportunity to reconsider the subject as he lay in a smallpox hospital in Constantinople.

I need scarcely dilate on the virtues of Treacher Collins as an ophthalmologist. One can read few articles on the eye in which his name does not appear. At the meetings of the British Ophthalmological Society his opinion was always listened to with special deference. He had the unique honor of being twice elected to its presidency.

During the aforementioned visit to Edinburgh I had some interesting talks with Ernest Maddox, and he was later kind enough to correspond with me on certain cases of unusual muscular involvement. His health

was never robust, and eventually he left Edinburgh for Bournemouth, a pleasant town on the South coast of England.

It was when confined to his bed or couch that he worked out the basis of his book on prisms. In his house in Edinburgh he showed me what he called the mother of the rod test. It consisted of two prisms bases touching. When held before one eye, the other eye being closed, it caused a candle light to appear in two positions, both false, joined by a line produced by the junction of the two prisms. When the other eye was opened a third flame, the true image, appeared.

The position that Maddox took on the question of the use of mydriatics in refraction was that it is more scientific to omit them because some of the hypermetropia of the large pupil may be due to the fact that the curvature of the cornea is greater at the periphery than at the center. After having tried both methods I personally believe that the best procedure is when possible to examine first with and later without a mydriatic, always concluding with both eyes open. This often means the addition of a quarter of a diopter or even much more to a plus glass, because the relaxation of the zonule produced by the mydriatic may permit a forward displacement of the lens, with a resulting temporary reduction of hypermetropia. Such a lenticular displacement probably accounts for the fact that not infrequently a higher plus glass is taken without a mydriatic than with one.

The zonule has been the subject of one of the most interesting researches in ocular physiology in recent years. In days gone by one of two theories of accommodation was accepted. Tscherning held that the strain of the zonule, or suspensory ligament, on the periphery of the lens by flattening the periphery actually caused its pupillary area to bulge. But the shape and refraction of a subluxated lens seemed to prove the other theory, that of Helmholtz, to be correct. He maintained that the lens tends of its own elasticity to become spherical. Yet one most important feature in the Helmholtz theory had always, at least to me personally, appeared most unsatisfactory; that is, that the choroid is drawn forward in order that the suspensory ligament may relax. Then came Thomson Henderson, of Nottingham, like his late fellow townsman Robin Hood, to shoot an arrow to the clout and knock ancient authority sky high.

In the Doyne Memorial Lecture at Oxford for 1926—which, incidentally, won for its author the Nettleship memorial prize—Henderson convincingly cleared up the puzzle. His research, prolonged and thorough, swept the field from the humble oyster to the king of beasts—I do not mean mankind, though one might, and Henderson investigated him too. For students who may not be familiar with this branch of Henderson's work I shall try in conclusion to summarize it in a few words.

The key to his investigations lay in his observation that the tense zonule does not pass from the lens outward in a straight line but is curved. If Helmholtz were correct this would seem contrary to nature. Henderson soon found, as was to be expected, that as the function of accommodation grows more complicated with the evolution of mammalian life so does its machinery. This is remarkably simple in the Herbivora, less simple in the Carnivora and considerably more highly developed in the Primates, including man. In the Herbivora, therefore, the scheme of accommodation is most easily demonstrated. It is well known that in fetal life the lens is practically a sphere that nearly fills the eye and that as the containing wall recedes the zonule needs must tighten up and compress the lens. But the lens or at least its cortex tends as long as it lasts to return to its pristine form. What prevents it? Henderson has shown that this persistent force is not the traction of the choroid but the tone of the ciliary muscle. If one imagines the zonule as a cord immovably fixed at one end to the cribriform ligament and at the other end to the lens, with the ciliary muscle inserted into the middle of this cord, one will have a rough picture of the anatomy of accommodation and understand how the traction on the zonule that flattens the lens must put a kink in the zonule.

But is such tonic muscular contraction in accordance with the laws of physiology? Here enters Sir Charles Sherrington's classic work on what he called the postural activity of muscle. He clearly demonstrated a noteworthy function of smooth muscle fibers. Smooth muscle is always supplied by both excitatory and inhibitory nerve fibers yet has the power of remaining static and at rest in any position set by these nerves without the further expenditure of nerve energy, like a rifle that is cocked or an old-fashioned window catch that is set. The ciliary muscle is thus locked and unlocked by the excitation of the sympathetic fibers and the inhibition of the fibers of the third nerve. This is precisely the reverse of the action of these fibers on the pupil and on the sphincter or the depressor fibers of the ciliary muscle.

Henderson at the same time demonstrated that presbyopia results not so much from a gradual loss of elasticity of the nucleus of the lens, whose cortex is continually being renewed, as from a marked and easily demonstrated sclerosis of the cribriform ligament and the fibers of the ciliary muscle which develops with advancing years.

Baldwin Heights.

CHANGE OF AXIS OF ASTIGMATISM ON ACCOMMODATION

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Estimating the error of refraction involves problems which are not commonly thought of during a routine examination but the recognition and the proper solution of which may be of extreme importance to the patient who presents the variation from the average. The purpose of this paper is to call attention to a rare condition which might easily escape detection, viz. a considerable difference in the axis of a moderate amount of astigmatism when the eyes are adjusted to the reading distance and when they are adjusted for distance fixation.

Since the first case was observed I have recognized 3 more and several other oculists have each recognized a similar one, their cases being included in the present report. This would indicate that the condition is not extremely rare, and one should be on the alert in cases in which the near vision is not as good as one would expect from the acuteness of the vision for distance, especially if the near vision is unequal, as in several of the cases reported here. Other factors of unequal accommodation, aniseikonia and ocular disease, such as the presence of central lenticular opacities, must of course be ruled out. The first case is reported in considerable detail to forestall criticism as to inadequacy of investigation.

This condition was first brought to my attention by a very intelligent patient, as reported in case 1.

REPORT OF CASES

CASE 1.—C. N. S., aged 45, a research engineer in the Bell Telephone Laboratories, had had considerable discomfort on use of his eyes for near work. He had noticed that through the reading segments of his bifocals the sight of the left eye was considerably better than that of the right and also that by rotating the right lens of his reading glasses considerably from the position prescribed he could see fine print which had previously been illegible and brought ordinary print into much better focus. An investigation on April 15, 1938 confirmed his observations. The following conditions were found:

The distance vision of the right eye was 20/15 + with +0.75 D. sph. \ominus +1.00 D. cyl. axis 155. With the addition of a +1.25 D. sph. the patient was able to read with difficulty 0.88 mm. type, the near point being 250 mm. and the far point 280 mm. Addition of more spherical power did not increase the ability to recognize small print.

On testing with a ± 0.25 cross cylinder with the eye fixed on a near vision chart at reading distance indication was found that a different axis was desirable for near range. The best vision was finally obtained with the same strength cylinder at 135 degrees, at which position there was a neutral response to the shift of the cross cylinder. It was also found that without change in the spherical strength of the presbyopic addition the visual acuity had increased to the ability to recognize 0.5 mm. type at a range of accommodation of 250 to 330 mm. Cross cylinder tests to determine strength were then done with this axis, and the same strength was indicated. Both a $+1.25$ D. cylinder and a $+0.75$ D. cylinder were rejected in favor of the $+1.00$ D. cylinder.

The $+1.00$ D. cylinder was then rotated 15 degrees in each direction from this axis (150 and 120 degrees). Each rotation resulted in a noticeable diminution of vision and of range, to the extent that 0.5 mm. type became blurred. The patient was requested to set the axis of the cylinder himself several times. This test confirmed the 135 degree axis for reading distance.

It was then thought that possibly the cylinder axis for distance was in error; so the spherical presbyopic addition was removed and the cylinder left at axis 135 degrees. The distance vision was found to be 20/30—. Cross cylinder tests, rotation settings of the cylinder by both examiner and patient and use of the astigmatic dial all repeatedly confirmed the previous strength and axis of the astigmatism for distance, at which axis, viz. 155 degrees, the vision of this eye was 20/15+.

The axis of the astigmatism of the left eye was found to be approximately the same for distance and for near vision. In this eye vision was 20/15 with $+1.50$ D. sph. $\ominus +0.75$ D. cyl. axis 15. With the addition of a $+1.25$ D. sph. the patient could recognize 0.5 mm. type, the near point being 250 mm. and the far point 300 mm.

Because of these unusual findings the patient was asked to return in eleven days for further testing, at which time the findings were confirmed.

The patient had separate reading glasses as well as bifocals; so the axis of the right reading lens was rotated to 135 degrees. No change was made in his bifocals, as it had not yet been proved that the condition was reasonably permanent.

He was seen again three weeks later, at which time the axis of the cylinder for the right eye was again found to differ for distance and for near vision. The plus axis preferred for distance vision was as before (155 degrees) and for near vision was 118 degrees. For the left eye the patient preferred a plus axis of 15 degrees for distance vision and of 180 degrees for near vision. He was asked to return in two months. On July 1 he was again tested, and the plus axes of the right eye of 155 degrees for distance vision and 120 degrees for near vision were confirmed. The axes of the left eye were 10 degrees for distance vision and 180 degrees for near vision. The reading lenses were adjusted to these axes, and a prescription for bifocals was given.

It is interesting to note the other findings brought out by the examination:

Exophoria of 2.00 prism diopters for distance vision and of 18.00 prism diopters for near vision was present, with hyperphoria on the left of 1.50 to 2.00 prism diopters. These anomalies had been observed when the patient was first seen, in 1936. Prisms totaling 3.00 prism diopters base in and 1.25 prism diopters vertically had been worn for many years. An examination for aniseikonia showed that the image seen by the right eye was 1 per cent smaller in the vertical meridian and 2 per cent smaller horizontally than that seen by the left.

The following prescription was given for bifocal glasses, which were made up with cement segments:

Distance: Right eye: $+0.75$ D. sph. $\bigcirc + 1.00$ D. cyl. axis 155 $\bigcirc 2.00 \Delta$ base in
 0.75Δ base up
 Left eye: $+1.50$ D. sph. $\bigcirc + 0.75$ D. cyl. axis 10 $\bigcirc 1.00 \Delta$ base in
 0.50Δ base down
 Reading: Right eye: $+1.75$ D. sph. $\bigcirc + 1.00$ D. cyl. axis 120 $\bigcirc 2.00 \Delta$ base in
 0.75Δ base up
 Left eye: $+2.75$ D. sph. $\bigcirc + 0.75$ D. cyl. axis 180 $\bigcirc 1.00 \Delta$ base in
 0.50Δ base down

To be made up in bifocal form.

The vision of each eye was 20/15 + for distance, and 0.5 mm. type was read at 250 to 330 mm. with each eye.

The patient was comfortable with the new lenses until one year later, when it was found that there was a change, particularly in the left eye. The following error of refraction was found:

Distance: Right eye: $+0.75$ D. sph. $\bigcirc + 1.00$ D. cyl. axis 148
 Left eye: $+1.50$ D. sph. $\bigcirc + 0.25$ D. cyl. axis 35
 Near range: Right eye: $+2.00$ D. sph. $\bigcirc + 1.00$ D. cyl. axis 130
 Left eye: $+2.75$ D. sph. $\bigcirc + 0.25$ D. cyl. axis 75

With these combinations the vision was equal with each eye for distance and for near vision.

A prescription was given for bifocals, the prismatic correction being the same as that previously given.

The patient has been treated recently for ulceration of the cornea and has had no complaints referable to his error of refraction, the prescribed lenses still being comfortable.

CASE 2.—Dr. E. C. J. was first seen in 1932, at the age of 45, when the following history was elicited:

He had had diplopia at the age of 10 years and had worn glasses for two or three years. Since then he had occasionally used a rest glass for reading. A chalazion had been present on the left lower lid and one on the right upper lid, both of which had been treated.

A slight twitching of the upper lid had been noticed for the past few weeks, especially during reading. The uncorrected vision of the right eye was 20/30—and that of the left eye 20/25; improvement to 20/20—and 20/15, respectively, was obtained with the following lenses: right eye, $+1.00$ D. sph. $\bigcirc + 0.25$ D. cyl. axis 80 (0.5 mm. type could be read at a near point of 150 mm. with each eye); left eye, $+0.75$ D. sph. $\bigcirc + 0.50$ D. cyl. axis 92.

The tension, the muscles, the media and the fundi were normal. There was a Mittendorf dot on the posterior surface of the right lens.

Two years later, July 29, 1934, the error of refraction was found to be as follows: right eye, vision 20/20 with $+0.62$ D. sph. $\bigcirc + 0.62$ D. cyl. axis 70; left eye, vision 20/15 with $+0.75$ D. sph. $\bigcirc + 0.75$ D. cyl. axis 90; near vision, ability to read 0.5 mm. type at a near point of 220 mm. with each eye; esophoria, 2.00 prism diopters; exophoria at near range (13 inches; 33 cm.), 6.00 prism diopters, and vertical deviation, absent.

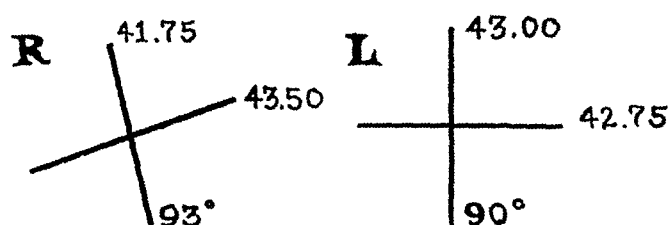
The same error was found one year later, April 7, 1935.

Five years later, July 12, 1940, the following error was found for distance vision: right eye, vision 20/15 with $+0.87$ D. sph. $\ominus +0.62$ D. cyl. axis 15 (with the addition of a $+1.50$ D. sph. 0.7 mm. type would be recognized) left eye, vision 20/15 with $+0.25$ D. sph. $\ominus +0.25$ D. cyl. axis 90 (with the addition of a $+1.50$ sph. 0.5 mm. type could be recognized). There were esophoria for distance of 4.00 prism diopters and exophoria at near range of 6.00 prism diopters, and the vertical muscle balance was normal.

With the plus cylinder of the right lens rotated to axis 75 degrees, 0.5 mm. type was readily distinguished as far as 270 mm. At the axis found for distance 0.5 mm. type could not be read. This error of refraction was confirmed by subsequent tests two months later. A prescription was given for reading lenses only since there were no symptoms referable to use of the eyes at distance.

This case was recognized by my associate, Dr. Byron C. Smith; I confirmed the findings at that time and on a subsequent visit.

CASE 3.—Miss Edna S., aged 18, had had esotropia since she was 3 years of age. She had worn glasses since she was $3\frac{1}{2}$.



The corneal measurements in case 3.

Vision was good in each eye, with the following error found by manifest refraction: in the right eye with $+2.50$ D. cyl. axis 8 vision was 20/20 and 0.5 mm. type could be read at a near point of 150 mm.; in the left eye with $+1.00$ D. cyl. axis 180 vision was 20/20 and 0.5 mm. type could be read at a near point of 90 mm.

Rotating the cylinder of the lens for the right eye to 18 degrees brought the near point in until it was the same as with the left eye and enabled the patient to read 0.5 mm. type with ease. A change from this axis for near vision resulted in diminished clarity of the print.

With refraction during homatropine-paredrine¹ cycloplegia the axes for distance vision were found to be the same as those obtained with manifest refraction. The corneal astigmatism was found to be as shown in the accompanying illustration. The corneal measurements did not change on accommodation and were the same before and during cycloplegia.

The patient had esotropia of 50 prism diopters for distance and for near vision, with defective fusion and alternating fixation. There was a small conjunctival nevus

1. The preparation of paredrine used was paredrine hydrobromide ophthalmic (p-hydroxy- α -methylphenethylamine hydrobromide, 1 per cent in distilled water, made tear isotonic with 2 per cent boric acid and preserved with merthiolate 1:50,000).

near the limbus at about 1 to 3 o'clock. Otherwise the external and internal examination of the eyes gave entirely negative results.

A prescription was given for two pairs of lenses, one for distance vision and the other for near work.

CASE 4.—Mrs. Ethel F., aged 39, complained of burning and a tired feeling in the eyes. The manifest refractive error was found to be: for distance vision, right eye 20/20 with +0.75 D. cyl. axis 30 and left eye 20/20 with +0.75 D. cyl. axis 150; for near vision, right eye +0.75 D. cyl. axis 75 and left eye +0.75 D. cyl. axis 150.

With cycloplegia there was no change in the strength or the axis of the cylinder of the left eye but for the right eye the patient preferred the same strength cylinder at axis 45 degrees.

Since the condition in the first case was recognized I have spoken to many colleagues and have twice reported this condition before the New York Ophthalmological Society. At a meeting on November 11, 1940 Dr. Rudolph Aebli² reported the following case:

CASE 5.—A young man struck in the right eye had traumatic mydriasis with rupture of some of the lower zonule fibers. The lens, the vitreous and the fundus were normal. The vision was 20/20 in the right eye with +1.25 D. cyl. axis 105 and 20/20 in the left eye with +1.25 D. cyl. axis 75. Accommodation was 0.5 D. less in the right eye than in the left. The patient complained of difficulty in reading and stated that the vision of the right eye blurred. Dr. Aebli prescribed +0.50 D. sph. \ominus 1.25 D. cyl. axis 105 for the right eye and +1.25 D. cyl. axis 75 for the left.

The patient read Jaeger test type no. 2 with difficulty with the right eye and Jaeger test type no. 1 with the left eye and still complained of blurring during reading.

After conversation with me, Dr. Aebli tried rotating the cylinder and found that the patient preferred it at 135 degrees in his reading glasses and with this axis could read Jaeger test type no. 1.

Dr. James Greear,³ of Washington, D. C., reported the following case, in which there were other factors, on account of opacities and irregular corneal astigmatism.

CASE 6.—Dr. J. F. R., aged 71, gave a history of having had ulcers of both corneas following measles at the age of 5 years, and he had some fine superficial scars of the cornea of each eye, slightly more marked in the right. Vision in the right eye was 18/200; with the addition of -0.75 D. sph. \ominus -1.75 D. cyl. axis 50 it was 20/50 -1 . Vision in the left eye was 20/50; with the addition of +1.50 D. cyl. axis 10 it was 20/30 -2 . The muscle balance both for distance and for near vision was essentially normal. The patient could read Jaeger type no. 1 at $8\frac{1}{2}$ inches (225 mm.) slightly better with the left eye with +1.50 and +1.00 D. spheres combined with the same cylinders.

He reported on May 29, 1933 that he could read more comfortably with the right eye with his glasses reversed. On October 26 his refraction was again

2. Aebli, R.: Personal communication to the author.

3. Greear, J.: Personal communication to the author.

checked. Vision in the right eye with -1.50 D. sph. $\ominus -1.75$ D. cyl. axis 60 was 20/50—. Vision in the left eye with $+1.50$ D. cyl. axis 10 was 20/30—. He read Jaeger type no. 1 at $8\frac{1}{2}$ inches (225 mm.) with the right eye with ease with $+1.50$ D. sph. $\ominus -1.75$ D. cyl. axis 160 and with the left eye with $+1.00$ D. sph. $\ominus +1.50$ D. cyl. axis 10. No change was made in his distance glass. The axis of the cylinder for the right eye was changed to 160 degrees. After this the patient was entirely comfortable.

His vision was checked again on July 12, 1940. Vision in the right eye was 20/200. With -0.50 D. sph. $\ominus -2.50$ D. cyl. axis 55 it was 20/40. Vision in the left eye was 20/70. With $+0.75$ D. sph. $+1.50$ D. cyl. axis 10 it was 20/40. He showed mild vertical muscular imbalance with mild esophoria both for distance and for vision. He could read Jaeger no 1 type at $7\frac{1}{2}$ inches (190 mm.) slightly better with the right eye when the correction was $+1.25$ D. sph. $\ominus -2.50$ D. cyl. axis 140 for the right eye and $+2.25$ D. sph. $\ominus +1.50$ D. cyl. axis 10 for the left. The following prescription was given:

Right eye: -0.25 D. sph. $\ominus -2.00$ D. cyl. axis 52 $\ominus 2.00$ Δ base out
 $+0.37$ D. sph. $\ominus +1.50$ D. cyl. axis 10 $\ominus 2.00$ Δ base out

Left eye: $+1.50$ D. sph. $\ominus -2.00$ D. cyl. axis 150
 $+2.12$ D. sph. $\ominus +1.50$ D. cyl. axis 10

Perhaps the patient's corneal opacities had some bearing on the error of refraction. One certainly would not expect him to have much accommodation remaining at the age of 70.

Dr. Avery Prangen⁴ wrote in reporting a somewhat similar case, "I know of no reference to this subject in the literature." His case, the first that he encountered, is presented as case 7.

CASE 7.—Mrs. P., who had a pseudoconical cornea with a high degree of mixed astigmatism, for about ten years wore two pairs of glasses in which the axes for the astigmatism were different for distance and for near vision. This difference was approximately 30 degrees for one eye and 20 degrees for the other.

The variation in the axes of the astigmatism had no relation to the conical cornea, since no other patient with the variation had any corneal abnormality.

Her latest manifest refraction, at the age of 50, showed that vision was 6/7—2 in the right eye with -1.00 D. sph. $\ominus -9.50$ D. cyl. axis 35 and 6/15 + in the left eye with -8.50 D. cyl. axis 120. For near vision nothing was added to this correction for the right eye and a $+1.00$ sphere was added for the left eye. It was found that for near vision the axis was 15 degrees in the right eye instead of 35, as for distance vision, and with a cylinder of this axis the vision was 14/14 with the American Medical Association near vision test card. The axis in the left eye was the same for both distance and near vision.

The patient had had typical low grade pseudokeratoconus ever since Dr. Prangen had known her. The results of examination with the Placido disk, the ophthalmometer and the retinoscope were typical. The condition remained stationary throughout many years, and the patient was able to obtain satisfactory vision with the highly astigmatic lenses prescribed, wearing the two pairs of glasses, one for distance and one for near vision.

4. Prangen, A.: Personal communication to the author.

Dr. John N. Evans⁵ reported a similar case:

CASE 8.—Examination with homatropine showed an error of refraction of + 0.75 D. cyl. axis 165. With fogging the vision with the same lens was $6/6 \times 3$. The patient could not use the lens at all for near vision until the axis was rotated to 90 degrees; then the vision blurred badly for distance.

Several other outstanding ophthalmologists who were questioned had not encountered any such cases.

Dr. Charles A. Drake⁶ reported having observed a similar case but gave no details. He thought the change in axis in his case was due to a slight rotation of the eye on looking down and in.

COMMENT

It is interesting to note that in all the cases reported the axis of astigmatism for distance vision was oblique. It is conceivable that in the act of accommodating the effect on the suspensory ligament of the lens is greater on a portion in line with one diameter of the lens than on a portion in line with another diameter, or that the lens matter in one sector may be more (or less) rigid than the remainder of the lens.⁷ Either hypothesis would explain the conditions found. The change in axis could not be due to rotation of the eye as a whole, as no abnormal torsion was seen with the unaided eye, with the microscope or with the ophthalmometer. The phenomenon must therefore be lenticular in origin. It is more remarkable that the axis of the astigmatism is usually the same for distance and for near vision than that a difference in the axis on accommodation is occasionally found. Discussing the work of Dobrowolsky, Duke-Elder⁶ stated that there is no scientific foundation for the claim that the accommodative effort of the ciliary muscle deforms the lens unequally in different meridians.

In designing bifocal lenses to correct the change in axis it is usually necessary to resort to cement segments.

This unusual condition may be the cause of discomfort on use of the eyes at near range, and its detection may result in considerable increase in efficiency and comfort for the patient.

I have been unable to find any reports in the literature of a similar condition, and none of the ophthalmologists with whom I have corresponded was able to refer me to a report of a similar case.

It is hoped that this presentation will stimulate further investigation into this interesting and unusual condition and that relief will be afforded patients who would otherwise remain unrelieved of their discomfort.

5. Evans, J.: Personal communication to the author.

6. Drake, C.: Personal communication to the author.

7. Duke-Elder, W. S.: *Text-Book of Ophthalmology*, St. Louis, C. V. Mosby Company, 1934, vol. 1, p. 749.

SUMMARY

Several cases are reported in which there was a change of the axis of astigmatism for near vision as compared to the axis for distance vision. The cause is presumed to be a sector weakness of the suspensory fibers of the lens.

NOTE.—It is my impression that this phenomenon may be due to a weakness in one portion of the suspensory fibers of the lens causing unequal effects on different meridians of the lens on accommodation, with resulting irregular change in the shape of the lens. This is particularly suggested by Dr. Aebli's case, in which a rupture of some of the fibers of the zonule was seen clinically.

RETINAL PERIPHLEBITIS IN THE COURSE OF ACUTE EXUDATIVE CHOROIDITIS

ARNOLD KNAPP, M.D.

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During the course of acute exudative choroiditis 2 patients presented periphlebitic changes in the retinal veins. These changes developed in the early stage, when the disturbance of the vitreous was pronounced; they remained stationary for some months and then cleared up without leaving any ophthalmoscopic changes in the veins. They affected only the retinal veins, and the veins were involved without reference to the location of the choroidal exudate. The veins were congested but not tortuous, and the perilymphatic sheathing was distinct, covering the veins like a veil. At regular intervals the sheaths presented ampulliform distentions, usually at right angles to the course of the vein. At these places the red color of the vein was masked so that the blood column appeared interrupted and the picture resembled that of a pussy willow. Some of the veins showed only sheathing, without the ampulliform dilatations. The arteries presented no anomaly. There were in addition diffuse preretinal opacities such as are seen when the disturbance of the vitreous is pronounced. These resembled the early changes which I described in an article presented before this society some years ago, changes which later in part become organized. They did not affect the ultimate vision, and after the choroidal exudate was absorbed the eye-ground showed no change beyond the usual cicatricial and atrophic choroidal area.

REPORT OF CASES

CASE 1.—E. M., a boy aged 15, seen on Dec. 15, 1939, had a history of failure of vision in the left eye for one month, beginning with spots and flashes, and the vision was reduced to 20/50. In the nasal periphery of the fundus there was a large exudate in the choroid, with opacities of the vitreous. On Feb. 2, 1940 the posterior corneal deposits and the opacities of the vitreous were unchanged but the temporal venous branches showed perivascular infiltration and sheathing. On February 26 other retinal branches showed a similar lesion. The veins were broadened with small superimposed white exudates like infiltrations of the lymphatic sheaths (fig. 1). On March 12 there was no change in the intraocular condition. On April 20 the vision was 20/50 and the retinal periphlebitis was unchanged. The patient then returned to his home in Colombia, South America, and he was not seen until Feb. 4, 1941, when the vision in the left eye was 20/40 — corrected with cyl. axis 30 to 20/20 —. There were some faint opacities in the vitreous, but the choroidal area was quiet and atrophic. The retinal veins were normal.

Read at the Seventy-Seventh Annual Meeting of the American Ophthalmological Society, Hot Springs, Va., May 29, 1941.

CASE 2.—A. E. W., a man aged 23, first seen on Sept. 22, 1934, stated that the vision in the left eye had been affected for two weeks; it was 20/70—. There were corneal deposits and many opacities in the vitreous. A fresh choroidal focus extending downward and outward near an old pigmented area could be observed. The retinal veins were dilated and presented many white spots in the walls, especially in the two nasal branches; these were similar to the exudates in case 1 but not as marked. The changes persisted for some months and then gradually cleared up. At a final examination, on Sept. 12, 1935, the vision was 20/20 and there were faint sclerotic changes in the retina in the macular area but the retinal vessels were apparently normal. A quiescent choroidal scar was present in the periphery of the fundus, extending downward and outward.

COMMENT

The causation in these 2 cases will not be discussed because in them, as in most cases of acute exudative choroiditis, the cause is not understood and the treatment followed had no effect on the periphlebitis.

This unusual complication of periphlebitis is interesting and can be studied from a number of angles. Knowledge of the lymphatic spaces that surround the retinal vessels is not definite. Eisler¹ stated that there are no lymphatic vessels either in the optic nerve or in the retina, and histologic investigations have not succeeded in demonstrating their presence. Eisler stated the belief that the spaces are like the sheaths about larger arteries which result from vascular pulsation. Such spaces are not lymphatic sheaths and are not lined with endothelium but are splits in the tissue which contain ordinary tissue fluid and not lymph. In the case of the retinal vessels the glia represents the connective tissue which forms a vascular sheath. Dr. R. K. Lambert, of New York, was kind enough to show me a histologic specimen from a normal retina, cut on the flat, which demonstrates the lymphatic sheath of a retinal vessel and is not regarded by anatomists as an artefact.

Koepe² with his slit lamp microscope saw lymphatic sheaths especially in the vessels on the papilla and in the case of certain morbid conditions of the retina found them dilated, sometimes with ampulliform dilatations. He stated that the veins as well as the arteries are regularly surrounded by perivascular lymphatic sheaths connected by a peculiar reticular framework and extending into the retinal structure.

Keller³ described the ophthalmoscopic changes which he observed in the retinal veins in a case of septic endophthalmitis and stated that this was the first case reported in the literature. These changes are

1. Eisler, P., in Schieck, F., and Brückner, A.: *Kurzes Handbuch der Ophthalmologie*, Berlin, Julius Springer, 1930, vol. 1, p. 152.

2. Koepe, L.: *Nernstpalatlampe und Hornhautmikroskop*, Arch. f. Ophth. **97**: 1, 34 and 198, 1918.

3. Keller, J. M.: *Retinal Periphlebitis in Septic Endophthalmitis and Its Ophthalmoscopic Picture*, Tr. Am. Ophth. Soc. **33**:520, 1935.

similar to those observed in the 2 cases reported, and this fact shows that such changes may be caused by a number of conditions in the presence of a severe disturbance of the vitreous. In Keller's case septic endophthalmitis followed a perforating injury of the sclera. A month after the injury the condition had cleared sufficiently to permit a view of the eyeground, and several small white, fairly well outlined, round disseminated spots were observed along the course of the retinal veins in the nasal half of the retina. More spots appeared and then disappeared in the course of a few days. A faint persisting turbidity of the vitreous and haziness of the lens remained.

Microscopic involvement of the sheaths of the retinal veins has been described in association with a number of inflammatory conditions of the eyeball.

Verhoeff ⁴ was fortunate enough to have an opportunity to examine histologically the blind eye of a patient suspected of having sympathetic uveitis in the other eye. The latter eye responded to treatment and recovered. In the enucleated eye there was observed a choroidal lesion consisting of epithelioid cells, giant cells, lymphocytes and plasma cells. Every retinal vein was surrounded by a mantle of lymphocytes. A nodule, or collection of epithelioid cells, was observed contiguous to every retinal vein and in other places without any relation to the vein. According to Verhoeff the minute tubercles scattered over the surface of the retina had been produced by macrophages derived from the primary lesion and deposited on the retina from the vitreous with a predilection for the retinal veins.

Fuchs ⁵ drew attention to the accumulation of lymphocytes around the blood vessels, within the lymphatic sheaths and chiefly around the veins in cases of ectogenic intraocular inflammation. He stated the belief that toxins coming from the vitreous act on the retina, causing dilatation of the veins and migration of lymphocytes, which accumulate in the perivascular lymphatic spaces. As the process becomes more severe the lymphocytes infiltrate the inner layers of the retina, though the periphlebitis rarely exists alone, like a separate disease.

In the presence of certain inflammatory processes in the anterior part of the uvea the pathologic agents may pass from the ciliary body along the perivascular lymphatic sheaths of the retinal veins, causing periphlebitis. This occurs particularly in association with tuberculous iridocyclitis and has been described by Meller, Verhoeff, Finnoff, Goldstein and Wexler and others.

4. Verhoeff, F. H.: Histologic Observations in Case of Localized Tuberculous Chorioretinitis, *Arch. Ophth.* **1**:63 (Jan.) 1929.

5. Fuchs, E.: Ueber Veränderungen des Sehnerven bei ektogener intraokularer Entzündung, *Arch. f. Ophth.* **91**:1, 1916.

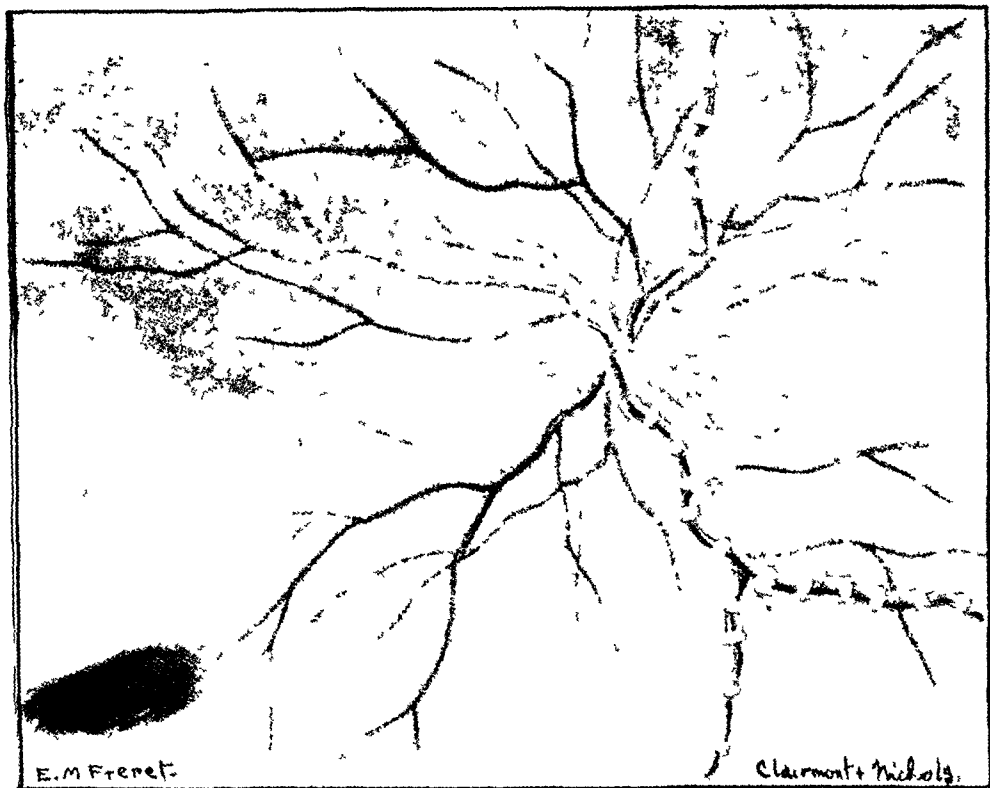


Fig. 1.—Retinal periphlebitis in acute exudative choroiditis.

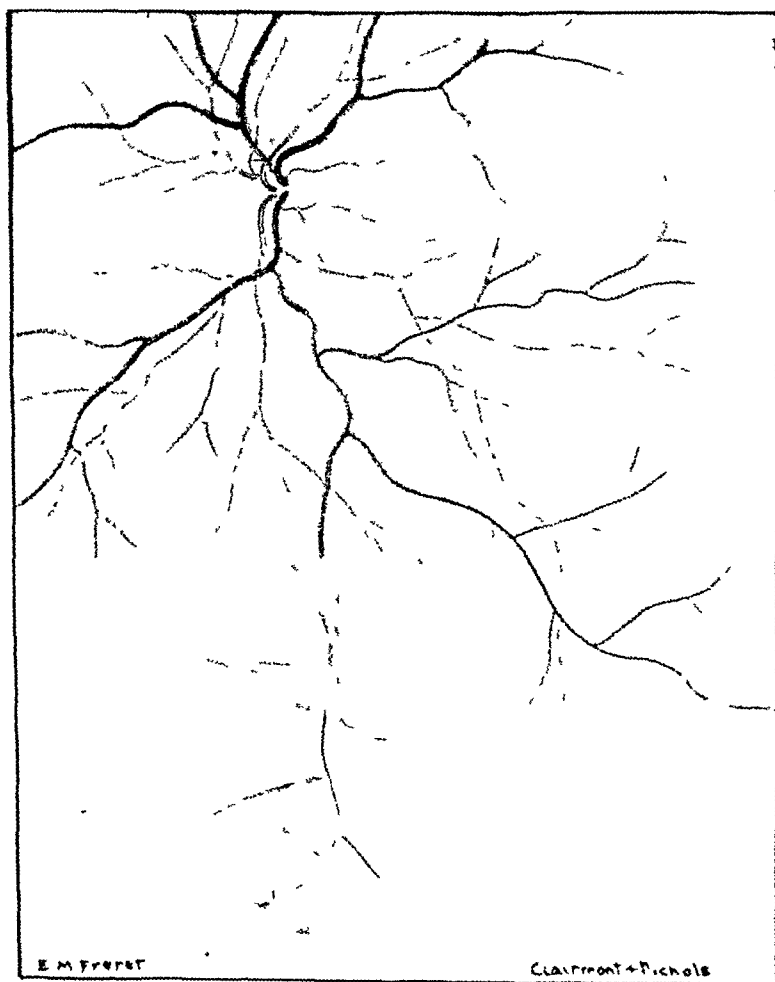


Fig 2—Hemorrhages of the vitreous of adolescents.

Axenfeld and Stock⁶ have shown that spontaneous hemorrhages of the retina and of the vitreous arise from tuberculous disease of the sheaths of the retinal veins. The anatomic proof has been presented by Gilbert, Fleischer, Hans Wolf and others. The tuberculous process is lodged principally in the lymphatic sheaths of the veins. The veins are surrounded by rings of lymphocytes, with epithelioid cells and giant cells, which distend the lymphatic sheaths and cause spindle-shaped ectasias. Hemorrhages are present in the surrounding retinal tissue and break into the vitreous. The arteries are invaded only where they cross periphlebitic foci. There may also be a formation like a whitish veil in front of the retina—a development of preretinal layers which may be vascularized and suggest the beginning of retinitis proliferans (Schieck).⁷

This is a different type of tuberculous infection, and Schieck expressed the opinion that histologically it resembles a tuberculous infection in an allergic person, which is characterized by an indifferent inflammatory tissue reaction and a tendency to proliferation of the supporting framework.

The ophthalmoscopic picture in cases of recurrent hemorrhages of the vitreous in adolescents, in which a periphlebitic process is present, is altogether different from the one described in this paper.

Some years ago I observed a man aged 23 with recurring hemorrhages of the vitreous. After a hemorrhage had been absorbed the following ophthalmoscopic picture was presented:

In the upper part of the periphery the course of a retinal vein was interrupted, a large whitish exudate rested on the lumen, broad infected lymphatic sheaths with numerous branches were visible and many hemorrhages and smaller exudates surrounded the course of the vessel and its branches.

Dr. Harry Friedenwald was one of the first to draw attention to this condition (fig. 2).

Finally, to return to my 2 cases, as the retinal veins nearest to the choroiditis were not particularly involved it seems rational to believe that the pathologic process coursed by way of the vitreous and that it must have been relatively mild since no permanent changes resulted in the veins, on the one hand, or in the retinal stroma, on the other.

6. Axenfeld, T., and Stock, W.: Ueber die Bedeutung der Tuberkulose in der Aetiologie der intraokularen Hämorrhagien und der proliferierenden Veränderungen in der Netzhaut, besonders über Periphlebitis retinalis bei Tuberkulösen, *Klin. Monatsbl. f. Augenh.* 49:28, 1911.

7. Schieck, F., in Henke, F., and Lubarsch, O.: *Handbuch der speziellen pathologischen Anatomie und Histologie*, Berlin, Julius Springer, 1928, vol. 11, pt. 1, p. 618.

LIME BURNS OF THE EYE: USE OF RABBIT PERITONEUM TO PREVENT SEVERE DELAYED EFFECTS

EXPERIMENTAL STUDIES AND REPORT OF CASES

ALBERT LOUIS BROWN, M.D.

CINCINNATI

The severe delayed effects of burns of the eye produced by certain chemicals are frequently unexpected because the initial injury seems to be *exceedingly minor*. Lime was chosen for these studies because it is used widely in industry, is frequently the cause of severe ocular destruction and in corrosive action is representative of the caustic agents which most commonly produce burns of the eye.

As a rule, when powdered lime (calcium oxide) strikes the open eye it adheres to the conjunctiva and cornea, part of it becoming dissolved in the tears. This becomes slaked lime (calcium hydroxide), which is as caustic as the powdered form. The tissues touched by the lime are immediately burned, as evidenced by redness and slight edema of the bulbar conjunctiva and a superficial whitish infiltration of the cornea. First aid treatment consists of irrigation, removal of particles of visible lime, instillation of a so-called neutralizing solution, such as 4 to 10 per cent ammonium chloride, and then application of atropine and a bland ointment. In a few hours the eye usually feels more comfortable; the conjunctival redness and swelling and the corneal infiltration seem to be simply manifestations of a local irritation. Two to three days later, however, the conjunctiva may be intensely swollen and the corneal infiltration more extensive, with perhaps some erosion of the corneal epithelium. At this time there is usually no lime to be seen and yet the ocular signs have become much worse. In a few days the conjunctiva may become grayish around the limbus and the cornea usually looks worse, because the limbal vessels have become obliterated and the nutrition of the cornea considerably impaired. The cornea may then heal with a dense scar or may slough completely, exposing the lens and the vitreous. Symblepharons usually are formed, and the lid may become attached to the cornea from the palpebral conjunctiva, with almost certain loss of the cornea. Thus the eye may be completely lost in from one to three weeks.

Read before the Section on Ophthalmology at the Ninety-Second Annual Session of the American Medical Association, Cleveland, June 4, 1941.

The prognosis in cases of severe burns of the eye treated conservatively, with irrigation, atropine and ointment, has been bad. Denig¹ has emphasized the need for some protective tissue after severe burns. He advocated the use of buccal mucous membrane placed on the globe after the removal of as much burned palpebral conjunctiva as possible. He claimed greatly reduced progression of the delayed reactions, and he is supported in this view by the more recent experiences of Theis and Neuman. Neuman² anesthetized eyes of rabbits and dogs and touched the bulbar conjunctiva with concentrated sulfuric acid, taking special care not to burn the cornea or sclera. In the first series, after producing a third degree burn in this manner he used conservative treatment and found that a delayed reaction occurred far more often and the final outcome was much worse than after the removal of burned conjunctiva and replacement by buccal mucous membrane. Other observers have used thin skin grafts, which seemed to lessen the severity of late reactions. Likewise, egg membrane has been used. This has not proved suitable, because such tissue becomes macerated quickly and will not retain sutures to keep it from slipping. Zenkina³ has used conjunctival transplants from cadavers for the same purpose.

Five years ago I used Denig's technic in 2 cases of severe lime burns. The eye seemed quiet after the transplants were placed, but the corneal erosion persisted. The grafts sloughed in four days, and symblepharon occurred. It seemed that the original burns were too slight to have caused all the late destruction, for the eyes never became quiet. Since the palpebral conjunctivas were very edematous and seemed to cause great discomfort, they were excised. Out of curiosity, I placed one of these conjunctivas in a rabbit's eye with the burned side against the cornea. The following day the cornea was hazy. The tissue was left and the lids sewed together. Each day the eye was observed and the cornea found to have become definitely eroded, with a central area of dense infiltration, as though it had been directly burned with lime. On the fifth day the tissue was removed and the lids simply closed again; the cornea healed with a dense central scar extending into the middle layers of the stroma.

The foregoing observation suggested that the burned palpebral conjunctiva in constant contact with the corneal surface acted as a corrosive agent and that a similar situation might occur after any severe burn.

1. Denig, R.: *München. med. Wchnschr.* **59**:579, 1912; *M. Rec.* **148**:395, 1938.

2. Neuman, J.: *Klin. Monatsbl. f. Augenh.* **95**:490, 1935.

3. Zenkina, L. V.: *Vestnik oftal.* (no. 2) **15**:28, 1938.

Severe lime burns of the skin do not as a rule show delayed reactions except so far as subcutaneous necrosis continues because lime is actually present. The initial burn is usually the extent of the injury, although healing after any chemical burn is necessarily slow because the immediate repair processes are hampered by local necrotic tissue.

The contrast of the reactions between a burned unopposed surface and two burned surfaces in contact was demonstrated in the following experiments. Three rabbits were placed under pentobarbital sodium anesthesia. The upper areas of the abdominal skin were shaved. These areas were burned with powdered lime and washed off with water in

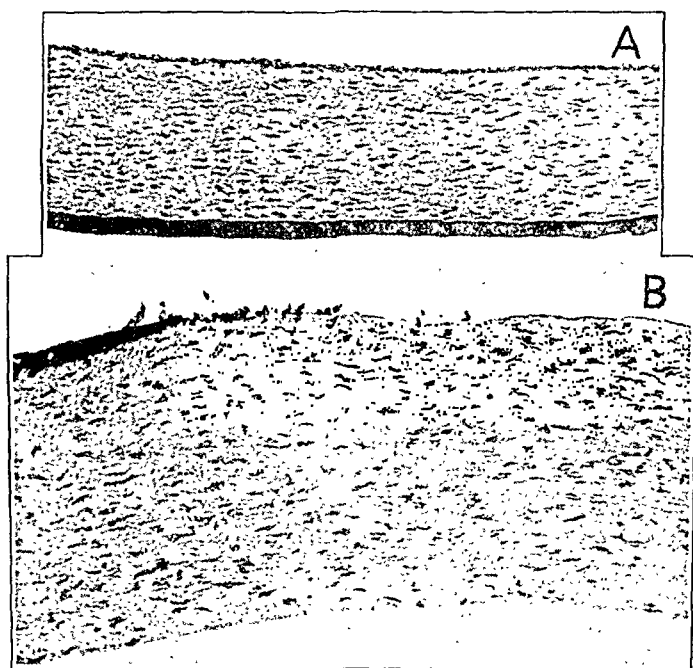


Fig. 1.—*A*, cornea two hours after direct application of lime. The epithelium is edematous, as are the upper layers of the stroma. *B*, cornea five hours after direct application of lime. There is desquamation of the epithelium, and the edema of the stroma has increased.

one minute. An unshaved area on each animal was burned and washed in a similar manner. Two opposing cutaneous surfaces in the right groin of each of the animals were burned with lime and washed off in one minute. The following day the burned areas of the shaved portions were slightly reddened, and they were fairly well healed in three days. The burned areas of the unshaved portions remained irritable and did not heal for approximately a week. This suggested that the smooth surfaces were more easily cleansed of all lime deposits, while the hairy surfaces retained particles of the chemical which could not be dislodged.

The two burned surfaces in the groins, which were allowed to rub against each other, remained irritable and did not heal for two weeks; there was considerable sloughing and an extension of the burned sites had started before healing began. This suggested that the rubbing of the two burned surfaces continued the irritation and prevented healing not so much because lime deposits were left but because the roughened and irritated surfaces irritated each other.

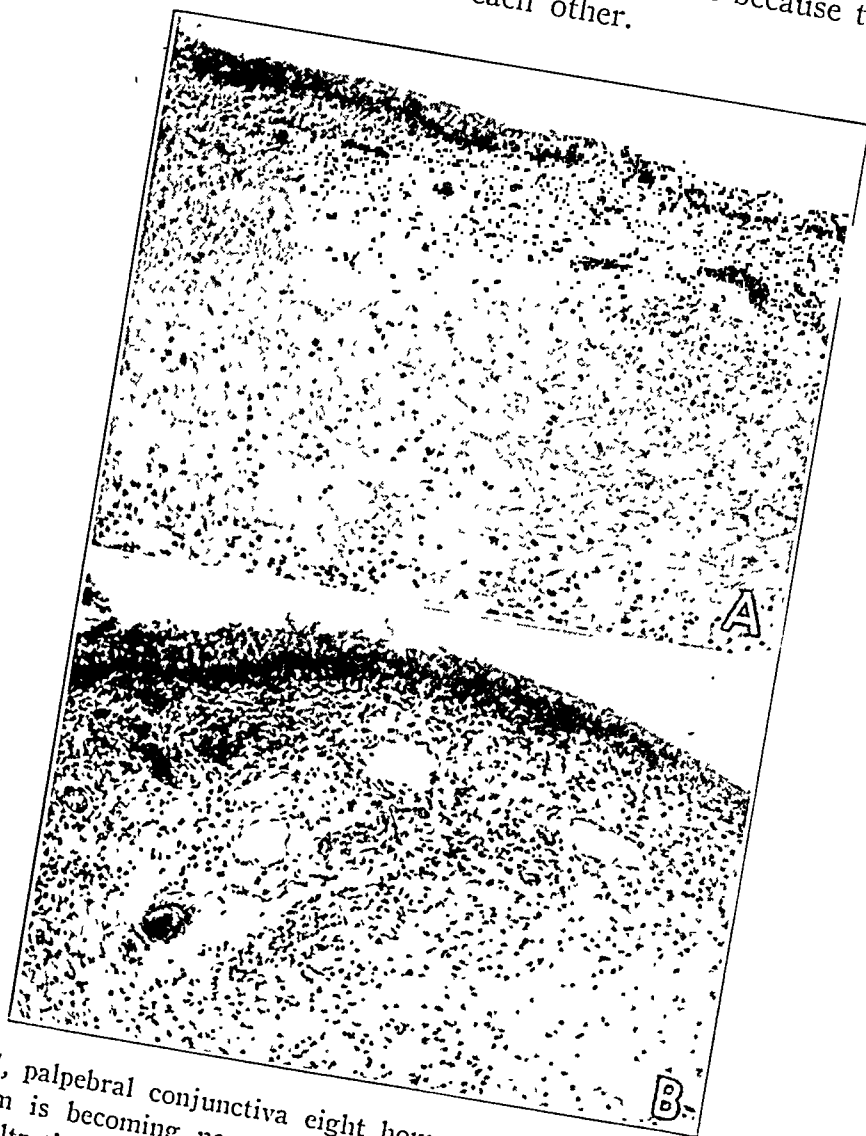


Fig. 2.—*A*, palpebral conjunctiva eight hours after direct application of lime. The epithelium is becoming necrotic, it is edematous, there are minute hemorrhages and infiltration with polynuclear cells is beginning. *B*, palpebral conjunctiva twenty-four hours after direct application of lime. All the signs shown in figure 1 have increased.

EXPERIMENTS ON RABBITS' EYES

EXPERIMENT 1.—*Lime Applied to the Cornea Alone.*—Two rabbits were anesthetized with pentobarbital sodium. The lids of the right eyes were held apart by retractors and gauze carefully placed to protect the lids and conjunctivas. With a fine camel's-hair brush a few particles of powdered lime (calcium oxide) were placed on the centers of the exposed corneas. A whitish area appeared on each

almost immediately. The lime was quickly washed away by water dropped in the eyes and immediately sucked up with a pipet to prevent spread in solution. The eyes were closed by a lid suture. In twenty-four hours there were small whitish corneal areas which stained in their centers and the bulbar conjunctivas were pinkish but not edematous. The palpebral conjunctivas were unaffected. Without treatment other than closure of the lids, the corneas cleared in five days without further spread of the erosion and without a scar.



Fig. 3.—*A*, palpebral conjunctiva thirty-six hours after application of lime; a section of the fornix showing advancing necrosis of the epithelial surface. Great edema and infiltration are present. *B*, deeper section of the tissues in *A*, showing edema to the orbicularis muscle.

EXPERIMENT 2.—*Severe Burns of the Conjunctiva but Not of the Cornea.*—Three additional rabbits were anesthetized with pentobarbital sodium. The right eyes were exposed by retracting the lids, and lime was placed on several areas of the lower part of each bulbar conjunctiva near the limbus. Care was taken to protect the corneas. The eyes were irrigated thoroughly one minute later. The

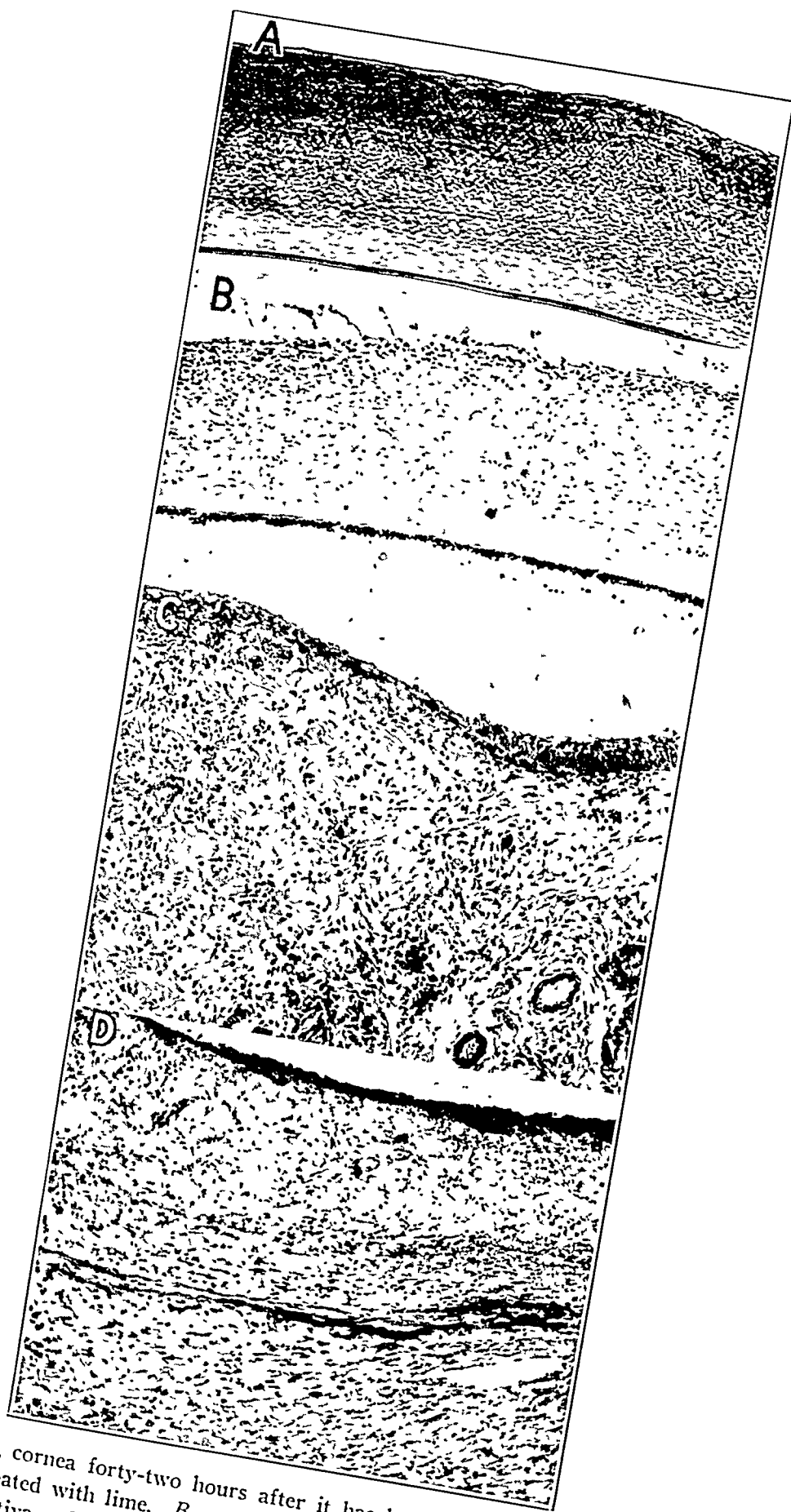


Fig. 4.—*A*, cornea forty-two hours after it has been in contact with palpebral conjunctiva treated with lime. *B*, cornea four days after contact with burned palpebral conjunctiva. *C*, lower part of the palpebral conjunctiva ten days after a lime burn. There is advanced ulceration, with beginning repair. *D*, section of the same lid, from near the fornix, with regeneration and cicatrization beginning.

bulbar conjunctivas became reddened quickly. One hour later there was considerable edema of the bulbar conjunctivas; the lids also became edematous. Twenty-four hours later the bulbar conjunctivas were very edematous and the corneas had slight superficial infiltration in the lower areas. In three days the edema was still severe but the corneas had cleared. The eyes were kept closed to insure uniform conditions. The conjunctival edema persisted for about ten days; the three eyes then became normal in appearance.

EXPERIMENT 3.—*Burns of the Palpebral Conjunctiva.*—Three additional rabbits were anesthetized. The everted palpebral conjunctiva of each right eye was treated with lime, and the surfaces were washed in one minute. Care was taken to protect the globes during this procedure. The burned surfaces became red almost at once. The lids were closed with a suture. Twenty-four hours later the palpebral conjunctivas were too swollen to allow eversion of the upper lids. After the lids were separated with retractors, the bulbar conjunctivas were found to be slightly edematous and the corneas infiltrated with a superficial central haze. One per cent atropine sulfate solution and 10 per cent boric acid ointment were instilled and the lids closed. Forty-eight hours later, the lids could be parted by fingers, but the corneas were more hazy although the conjunctivas were less edematous. The corneas took no stain at this time. In seventy-two hours the bulbar conjunctivas had lost most of the purplish discoloration and edema. The palpebral tissue was swollen and rough, and there were many sloughing areas. The corneal areas were definitely eroded and took a stain. From this time the conjunctival edema, both palpebral and bulbar, became less and small whitish areas of conjunctival scarring appeared near the limbus. On the fifth day the process in each of the eyes seemed to have reached its height. The change from day to day thereafter was slow. Two weeks after the initial injury each cornea had a dense central scar which could be stained faintly. Each rabbit had a permanent central corneal scar. The bulbar conjunctivas were fairly normal, and there was considerable scarring left in the palpebral tissue.

Since it was noted that the burned cornea healed in a reasonable time when protected by smooth palpebral conjunctiva and that a severely burned palpebral covering of itself could cause corneal erosion, a smooth protecting membrane between the two surfaces seemed necessary. Several membranes, such as oiled silk and thin rubber tissue from a rubber glove, were tried. These did not seem ideal, because they were too thick, caused irritation or were not sufficiently pliable. Rabbit peritoneum, which is easily obtainable in sufficiently large strips, proved to be the tissue of choice.

EXPERIMENT 4.—*Use of Peritoneum in Rabbits' Eyes.*—The right eyes of 5 rabbits under anesthesia were treated with lime, no effort being made to protect the surfaces. The eyes were irrigated thoroughly in one minute. Severe burns resulted. Strips of rabbit peritoneum were sewed into the upper and lower fornices, so that the bulbar and palpebral surfaces were separated. The period of edema and corneal erosion transpired and in five days was fairly well over. The peritoneum was removed on the sixth day in 1 rabbit. A dense corneal scar which did not

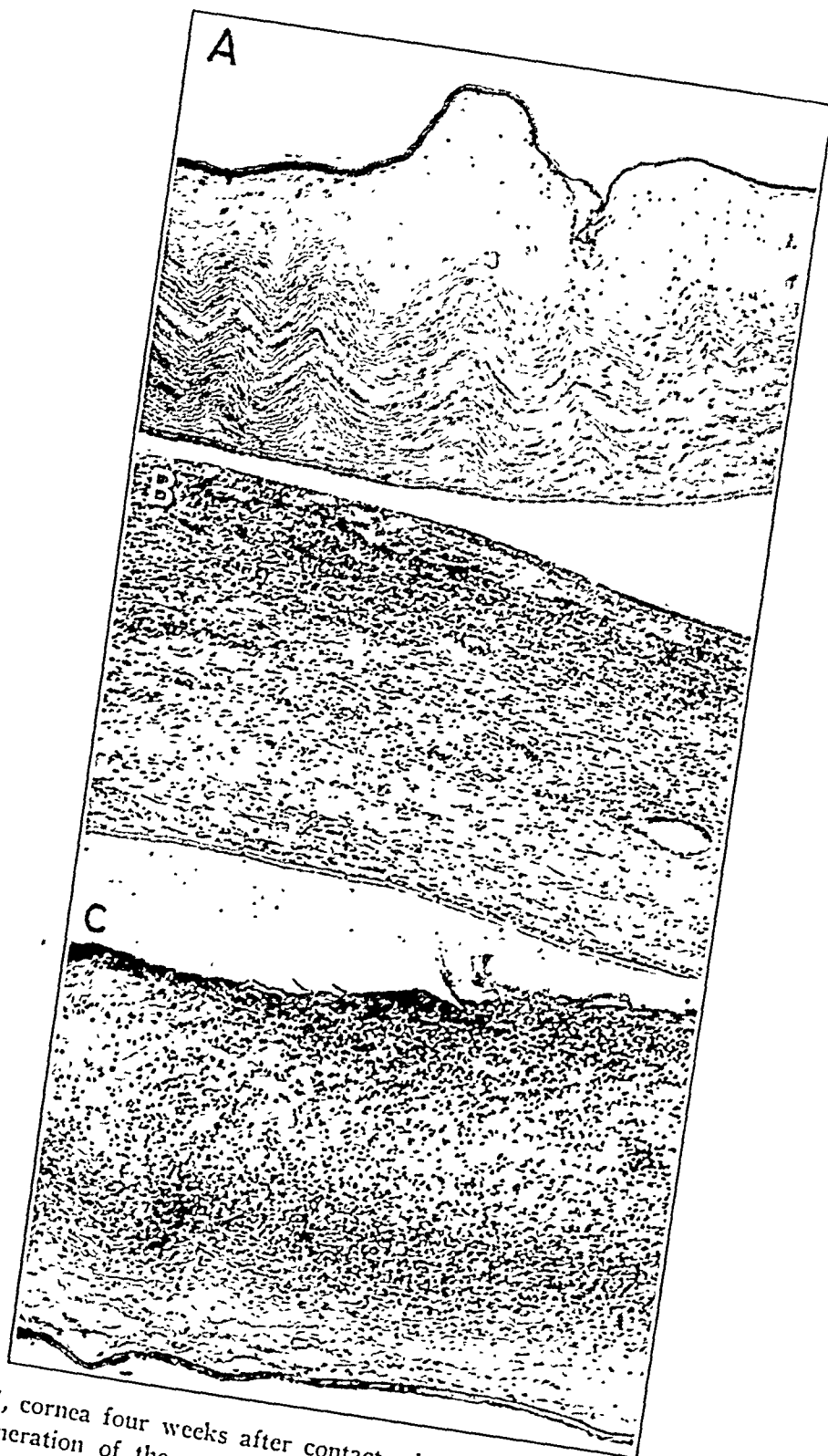


Fig. 5.—*A*, cornea four weeks after contact with burned palpebral conjunctiva, showing regeneration of the corneal epithelium, edema of the stroma and some fibroblastic repair. *B*, section of a similar cornea, showing vascularization and some repair. *C*, cornea seven weeks after contact with burned palpebral tissue. There are erosion, infiltration and some repair and vascularization.

stain was present. The following day the transplant was removed from another rabbit, and each succeeding day to the eleventh another transplant was removed. The final results in all the rabbits showed without question that although there were corneal scars they had not progressed or become as deep as those which developed when the surfaces were not protected.

REPORT OF CASES

CASE 1.—M. H., a workman aged 36, was splashed in the right eye while working with lime. The employer irrigated his eyes with water. Since the patient felt no immediate discomfort, he continued working. Five hours later the right eye burned intensely and felt as though he had "hot sand" in it. He was seen about six hours after the injury. At this time his lids were edematous but could be easily parted. There were great lacrimation, conjunctival edema and redness. A small whitish superficial infiltration was present in the lower portion of the cornea. The palpebral conjunctiva was swollen and contained a few lime deposits. All visible particles were removed, and atropine ointment was instilled and a bandage applied. The man was hospitalized. He was seen about fourteen hours later, at which time the lids and conjunctiva were more swollen. The corneal area was larger, and the surface could be stained. The patient was prepared for operation; a rabbit was killed with ether, and through a midline incision in the rabbit's abdomen a strip of peritoneum 4 by 10 cm. was excised. The tissue was folded and sewed into the upper fornix and placed over the globe loosely, and a lower fold was sewed into the lower fornix. The free ends were allowed to hang out between the upper and the lower lid. One per cent atropine sulfate solution was dropped behind the flap; no bandage was applied. The eye was irrigated three times a day with physiologic solution of sodium chloride. The second and third day the conjunctival edema was rather intense but the flap did not seem to be disturbed. Thereafter the discomfort diminished, so that the patient required no analgesic by the fourth day. On the sixth day the flap was turned out so that the cornea could be seen. The whitish area, which had seemed destined to become greatly eroded, had diminished to a small dot. The pupil was widely dilated, and the pupillary area was clearly visible. Since the flap was causing no irritation and the bulbar conjunctiva was still edematous and sloughing, the flap was left in place. Fourteen days later the palpebral conjunctiva seemed quiet. Since the flap was becoming macerated, it was removed. The eye made an uneventful recovery, except that there was slight cicatricial entropion of the lower lid without symblepharon. The final vision was 20/30.

CASES 2, 3 and 4.—A. L. (aged 40), B. C. (aged 46) and N. R. (aged 36), three workmen, were severely burned when a blower was suddenly turned on in the boiler in which they were working, blowing lime directly into their faces and eyes. They were met at the hospital about one hour after the accident. The face and eyelids of A. L. were severely burned, the conjunctivas were swollen and the corneas were already whitened. Rabbit's peritoneum was immediately placed in both eyes. B. C. was less severely burned, but a considerable amount of foreign material was washed and picked out of both eyes. The immediate burns did not seem sufficiently severe to warrant transplants. This was an error, because the next day the palpebral conjunctiva of the right eye was very edematous.

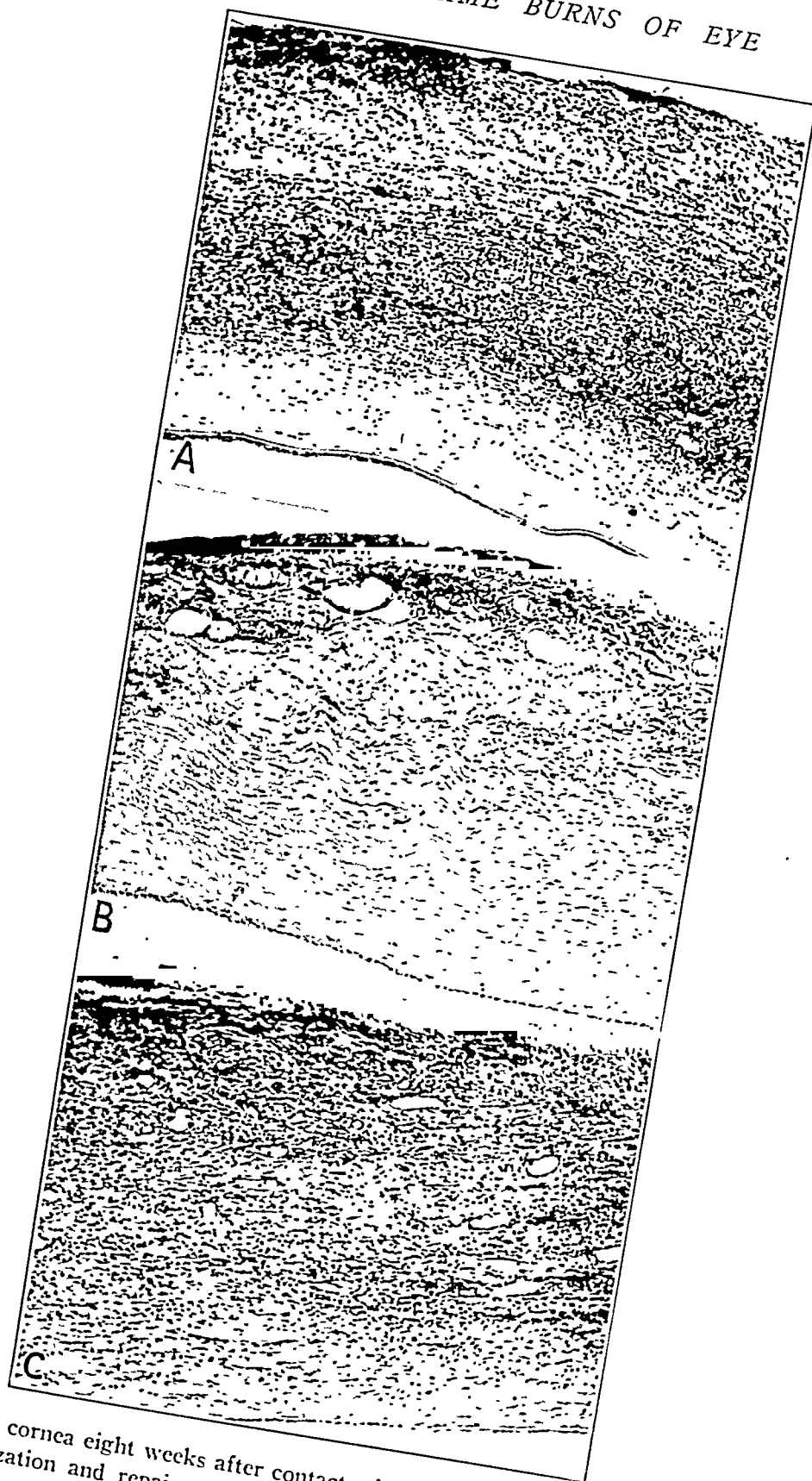


Fig. 6.—*A*, cornea eight weeks after contact with burned tissue, showing infiltration, vascularization and repair. *B*, ten weeks after contact cicatrization. There is considerable vascularization. *C*, section of a similar cornea, from near the limbus, showing advanced cicatrization.

and was acting as a typical corrosive element, rubbing against the cornea. There was a large whitish area in the right cornea, which already showed erosion. The peritoneal transplant was immediately placed, and although the edema became greater, the corneal erosion remained limited and healed, leaving a small scar. The left eye was not affected. The left eye of N. R. was badly burned and was immediately protected by peritoneum. The cornea was never affected. However, a symblepharon formed in the upper fornix where a part of the transplant pulled loose from the fixing suture.

These 3 cases presented an unusual opportunity for study of the use and efficacy of a tissue transplant. I am convinced that the second patient (B. C.) would have lost his right eye had it not been for the

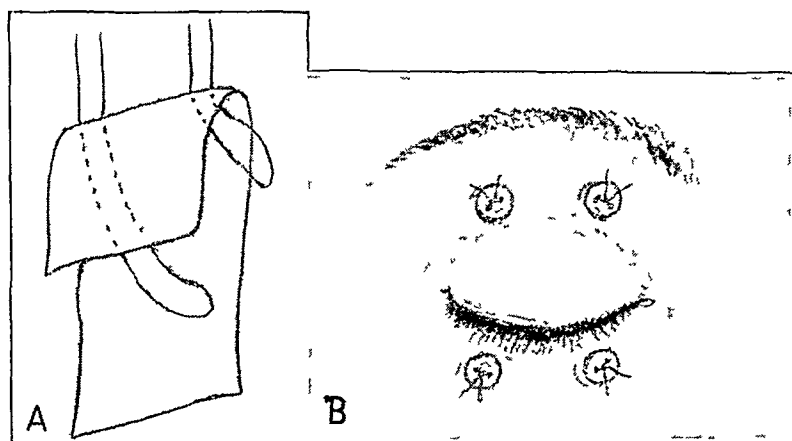


Fig. 7.—*A*, sutures through the peritoneal flap. *B*, the flap in place; position of the sutures and buttons.

timely recognition of the fact that this eye was going to present a delayed reaction and the consequent protection of the surfaces.

TECHNIC OF TRANSPLANTATION OF RABBIT PERITONEUM

Before the operation the extent of the damage should be determined, the eye carefully irrigated with warm water and all visible particles removed. Neutralizing solutions are of no avail unless used instantly and are better left out of the treatment because they may add further chemical irritation. If the lids are too swollen to permit a reasonable inspection, a wide external and even internal canthotomy may be done. A well grown rabbit is destroyed by ether, the midline of the abdomen shaved from the sternum downward and a midline incision made exposing the peritoneum. A section of peritoneum about 4.5 by 10 cm. is removed and passed through three successive washes of warm physiologic solution of sodium chloride. The needles of two double-armed no. 5 silk sutures are passed through the center area of the tissue

about 2.5 cm. apart. The needles are then passed through the upper fornix, emerging under the brow. The tissue is shoved gently into the upper fornix with a bone spatula and the sutures pulled along to help. When the tissue is placed as far up as possible, the sutures are tied over buttons to prevent their cutting through the skin. The tis-

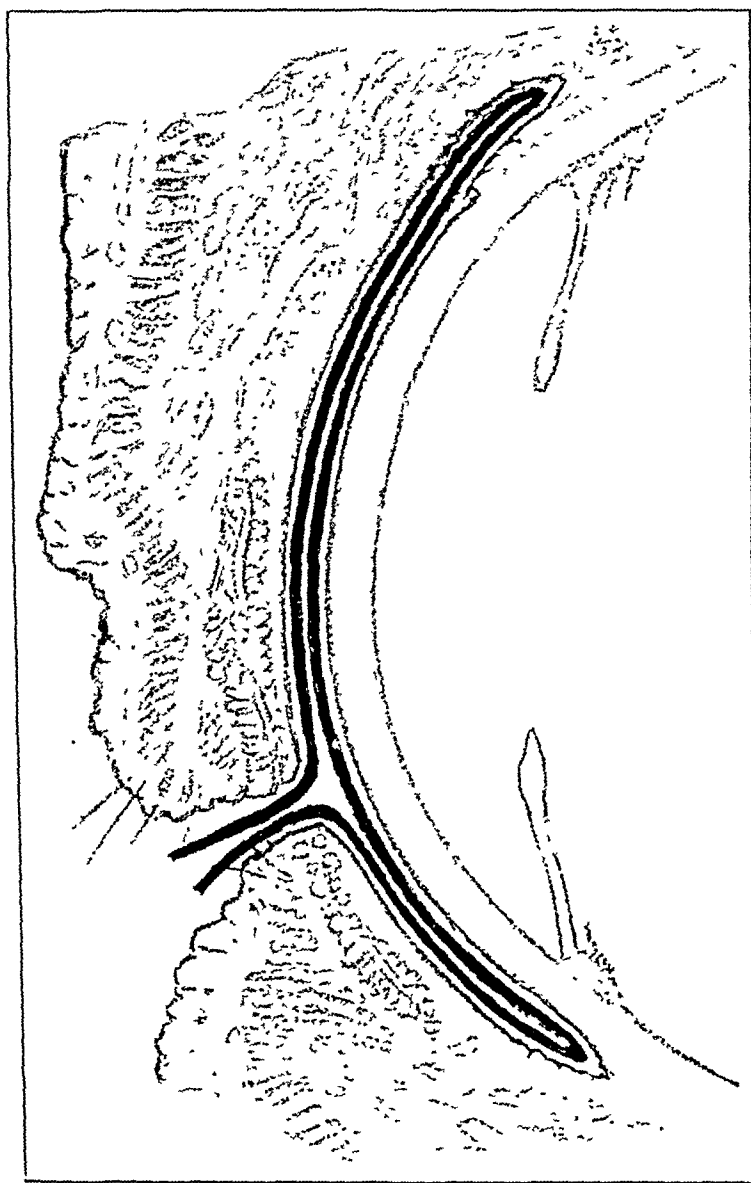


Fig. 8.—Side view of the flap in position.

sue is smoothed out over the eye and similarly sutured in the lower fornix, considerable play being left in the flap to allow for shrinkage. This procedure allows a doubled, smooth membrane to cover the entire eye and separate all opposing surfaces. The ends are permitted to hang out, and no bandage is applied. Any medication or irrigation indicated may be applied beneath either surface of the flap. The outer edge of the flap may be raised for observation of the cornea. When

it is released it will fall back in place. The flap is removed when the cornea is healed and the palpebral conjunctiva seems quiet. The time for this is usually two weeks after a severe burn, but it is usually best to leave the flap for three weeks or longer if no reaction or infection is manifest. The flap may be replaced whenever it becomes macerated or begins to shred.

As a rule no reaction follows the placement of this tissue. If an allergic or other reaction occurs, the flap may be removed, and thin oiled silk or a section of rubber glove may be substituted, but these coverings cannot compare in neatness, smoothness and pliability with rabbit peritoneum.

COMMENT

The foregoing experiments and cases seem to indicate the production of a chemical alteration in the palpebral conjunctiva from a lime burn. The altered membrane acts as a reservoir of corrosive substance which cannot be seen or washed off but continues the eroding action of the original lime. Furthermore, this swollen and usually partially macerated tissue is so irritating to the cornea as to act as an independent agent in preventing healing of the corneal epithelium. Thus, when the cornea is first burned washing with water simply puts some of the lime in solution. The visible particles may be removed, but the initial damage has been done in the first few minutes. If the cornea and the palpebral conjunctiva are separated by a smooth membrane, further irritation between the two most greatly affected surfaces is reduced to a minimum. Besides, the burned surfaces of the palpebral and bulbar conjunctivas must be separated to prevent symblepharon. The sheet of rabbit peritoneum serves several purposes by forming a smooth covering for two opposing raw surfaces which must be kept apart until healing is well advanced. The use of Denig's buccal mucous membrane graft is the closest approach to a rational attempt to separate and protect the burned areas. However, Denig's graft is placed on a macerated and often quickly infected area and frequently sloughs, leaving a wider area of erosion, which subsequently ends in greater cicatricial distortion and does not prevent symblepharon. Skin inlays are too rough, and they slough because of the underlying tissue, which cannot form a healthy or firm base. The rabbit peritoneum is not a graft but a protective covering to allow healing and therefore does not depend on the underlying tissues but protects them. After the first stage of healing, i. e. epithelization of the cornea with no staining, which should occur in four to eight days, the peritoneum has usually shrunk and begins to strip off in places. It rarely adheres firmly to the ocular tissues and can be removed with ease even after three weeks. If the peritoneum can be kept in place until the second stage of healing, i. e.

when swelling of the conjunctiva has abated and the surfaces are relatively smooth, even though scarred, the dangers of further erosion of the cornea and of symblepharon are usually passed. The flap may now be removed and the eye treated with atropine and ointment according to the indications. The removal or repair of scars should not be attempted until several months later, depending on the indications.

CONCLUSIONS

1. Conservative treatment of severe lime burns with ointment or drops is worthless in preventing delayed corneal erosion and symblepharon.

2. Experiments on rabbits suggest that chemical alteration of the palpebral conjunctiva in contact with the cornea is harmful.

3. The delayed severe corneal erosions after lime burns are usually due to the caustic effects of burned palpebral conjunctiva in contact with the cornea.

4. Affected surfaces must be completely separated by smooth tissue to allow healing.

5. Rabbit peritoneum seems to answer all needs for a protective membrane.

6. The use of this substance should be efficacious after most corrosive chemical burns.

ABSTRACT OF DISCUSSION

DR. EUGENE L. BULSON, Fort Wayne, Ind.: Ophthalmologists are aware of the severe delayed effects, often out of all proportion to the apparent severity of the original burn, sometimes produced by the action of a caustic in the eye. That these results are due to the inability to remove the offending agent completely from the tissues of the eye has been demonstrated by Dr. Brown's experiments. He has also clearly shown the severe escharotic action and delay in healing produced by the action of a caustic on unprotected contiguous surfaces, as compared with the relatively mild reaction occurring in tissues not in apposition. Application to the eyeball of a protective covering which will serve also to keep opposing surfaces separated seems to be not only the logical form of treatment but a necessary precaution if the severity of the sequelae is to be minimized. Skin grafts and transplants of various kinds have not been altogether satisfactory. In an attempt to prove to my own satisfaction the efficacy of Dr. Brown's method, I performed some of his experiments on rabbits' eyes, using peritoneal implants as a protective covering. Three rabbits were anesthetized with pentobarbital sodium, and a small amount of powdered lime (calcium oxide) was dusted into the six eyes. No other treatment was given to the three left eyes. A strip of fresh rabbit peritoneum wide enough to cover the eyeball completely and long enough to be tucked and sutured into the upper and lower fornices in a double fold was

placed in each of the right eyes according to the technic described by Dr. Brown. In all cases there was less scarring of the conjunctivas in the eyes protected with implants than in the unprotected eyes.

In a second experiment, with 3 additional rabbits, a larger amount of lime was used in each eye and it was allowed to remain for a longer period. On the seventh day the erosion of the corneas in the right eyes, which had been protected as in the first experiment, did not seem to be as deep or as extensive as that in the left eyes. At the end of two weeks there were large, dense white scars on the corneas of the left eye and the lids were distorted as a result of extensive scarring and the formation of adhesions. While there was permanent scarring of the corneas in the right eyes, it was not as dense or as extensive as it was in the unprotected eyes. The conjunctival changes were definitely less evident in the eyes in which the implants were used.

The ultimate outcome in the second experiment was even more striking than it was in the first, probably because the eyes in the second experiment received much severer burns. The results show without a doubt the value of a protective covering in preventing severe delayed reaction from burns of the eyes with caustics.

Peritoneal implants offer many advantages over skin grafts and other tissues; they are easily obtained, remain in place better, will not slough, because they do not depend on the underlying tissues for nourishment, and afford complete protection to the ocular structures. It should be remembered that the implant is not a graft in any sense of the word but is merely a protective covering of the eyeball which prevents the burned areas from coming in contact with each other and with healthy tissue. Rabbit peritoneum seems to be suitable. It is both easily obtained and easily prepared, and it should prove to be a valuable adjunct in the treatment of severe burns of the eye.

The best results are obtained with the thinnest strips of peritoneum it is possible to cut. In my first experiments I used thicker strips, and I believe that they are harder to handle, are more difficult to keep in place and may have a tendency to cause irritation.

DR. ROBERT J. MASTERS, Indianapolis: Dr. Brown has presented material of great interest, since lime burns of the eye are so inclined to produce tragic results that any promising form of treatment arrests attention.

Shortly after reading this paper, I treated a patient with lye burns of both eyes. I followed Dr. Brown's method, but the implants were too thick, including fascia and muscle in addition to peritoneum. They were apparently irritating to the corneal tissue and were removed after two days.

Experiments on the eyes of 5 rabbits followed. Dr. Mary Alice Norris and Dr. M. Mann, residents in ophthalmology at the Indiana University and Indianapolis City hospitals, assisted. Three rabbits were treated with slaked lime and 1 with unslaked lime, the material being dusted indiscriminately into both eyes and allowed to remain for three to ninety minutes. The eyes were then carefully cleansed, and one eye was treated by implant, the other remaining untreated, as a control. In each rabbit pronounced inflammatory and degenerative

changes developed in the cornea of the treated eye, while the untreated eye healed with moderate or no corneal scarring. One eye of the fifth rabbit was treated by implant, the other eye being left untreated, as a control, with no preliminary exposure of the eyes to lime. The treated eye of this rabbit exhibited corneal necrosis. (Slides of all the eyes were shown.)

In all the experiments the implants were isolated and sutured in place under careful surgical asepsis. Having learned by my mistake in the operation on my patient, I was careful to isolate thin strips of peritoneum containing no other tissue. Cultures were made of material from both eyes of each subject, but the results were not significant. Care was exercised to place the visceral surface of the peritoneum against the conjunctiva and the cornea.

The premise on which Dr. Brown's proposed treatment is based seems entirely sound. This is true of the other therapeutic measures which he has given to the medical profession. The protection of the cornea from the abrasive action of a damaged palpebral conjunctiva represents a good principle of treatment. It seems, however, that some other thin protective membrane should be substituted for rabbit peritoneum, since the latter has exercised a deleterious effect on the cornea in my small experience with it.

DR. ALBERT L. BROWN, Cincinnati: It is rare for two discussers to take the time and the trouble to go so thoroughly into the subject. Both of them particularly mentioned the immediate or early edema of the lid after the implantation of rabbit peritoneum. I mentioned that this occurs no matter how thin the peritoneal implants are. I hope I shall have an opportunity to discuss it later with Dr. Masters. I believe that his implants were much too thick. As soon as the implant strikes the secretion of the eye and the tears, it undoubtedly swells if there is any fascia or muscle tissue attached. The peritoneal tissue alone is not so apt to swell; it is almost inert with regard to swelling in fluid. I investigated different fluids that in p_H approximate tears, and I found that if a piece of peritoneal implant had aponeurotic fascia or muscle attached to it, it swelled in twenty-four hours to almost six times the original size. A criterion for the preparation of a peritoneal implant, therefore, is that it must curl when it is laid on a flat board. It must be tissue paper thin. The only way I know to remove such a piece is to dissect the entire wall, turn it inside out, have an assistant hold the muscle tissue with a pair of hemostats and then dissect it out. A piece big enough to use in a normal human eye takes fifteen to twenty minutes to prepare.

I am not sure that peritoneal tissue is the final choice, but I am satisfied that the two opposing surfaces must be separated by an implant rather than a graft and must be kept separated if possible until the second stage of healing has ensued.

Dr. Pascal has asked what advantage this method has over the application of large contact bands filled with a suitable medicament. I do not know. I have never used a contact glass in such cases, but I have used metal implants which I attempted to mold to fit exactly the fissure and the surface of the globe, and I found that the patient was unable to bear any kind of a resistant metal.

HYDROGEL QUALITIES OF THE VITREOUS

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NEW YORK

It is known that a large part of the vitreous fluid is water bound by capillary attraction and ready to escape when the vitreous is injured. Only a small amount of the fluid is colloiddally bound to the substrate of the fibrils as hydration water. These conditions explain the primary difference in the results of volumetric investigations with varying technics. For reasons mentioned in a previous paper¹ the vitreous should be examined in toto. Important as observations on the expansion of isolated fibrillar substance may be, it is of course not feasible to draw conclusions about volume changes of the vitreous from them. In the more frequently used method of recent investigators, pieces were cut from different parts of cattle vitreous and were found to decrease steadily in a physiologic milieu. This decrease, probably caused by the uncontrolled escape of capillary fluid, was prevented in our experiments by avoiding any serious injury to the vitreous (pigs' and human); that is, by leaving the ciliary body, the posterior part of the lens capsule and a thin layer of the optic nerve, with the retina, in place. Such vitreous preparations expand in physiologic solutions of sodium chloride, and the expansion can be studied under different conditions.

Recently reported experiments¹ demonstrated the amount of swelling of protected pigs' vitreous in isotonic buffered solutions of different hydrogen ion concentration. The volume curve differed from the curve of volume loss reported by Baurmann and Thiessen,² Duke-Elder³ and Goedbloed.⁴ Baurmann and Thiessen deduced the gel nature of the

Supported by the Knapp Memorial Foundation.

From the Department of Ophthalmology, Columbia University College of Physicians and Surgeons, and the Institute of Ophthalmology, Presbyterian Hospital.

1. von Sallmann, L.: The Expansion Tendency of the Vitreous and Its Volume Curve, *Arch. Ophth.* **25**:243 (Feb.) 1941.

2. Baurmann, M., and Thiessen, A.: Die Struktur im Glaskörper des Auges, *Nachr. v. d. Gesellsch. d. Wissensch. zu Göttingen., math.-physik. Klasse*, 1922, p. 125; cited by Goedbloed.⁴

3. Duke-Elder, W. S.: The Physico-Chemical Properties of the Vitreous Body, *J. Physiol.* **68**:155, 1929; The Vitreous Humor, *Tr. Ophth. Soc. U. Kingdom* **49**:83, 1929; The Nature of the Vitreous Body, *Brit. J. Ophth.*, 1930, supp. 4, p. 1.

4. Goedbloed, J.: Studien am Glaskörper, *Arch. f. Ophth.* (a) **132**:323, 1934; (b) **133**:1, 1935; **134**:146, 1935; **137**:127 and 131, 1937.

vitreous from the resemblance of its curve to the turgescence curve of some ampholyte gels. Goedbloed disagreed with their interpretation because of the implication that changes in the electric charge were responsible for the different degrees of loss. He explained the loss in volume in strongly acid ranges as the result of coagulation of the mucoprotein in the form of filaments, which, as they draw together, mechanically press out the fluid; he considered the decrease in volume in strongly alkaline ranges as due to the dissolving action of alkalis on the framework.

The volume changes of hydrogels in solutions of different hydrogen ion concentration are characteristically reversible. Goedbloed found, how-

TABLE 1.—*Volume Changes in Distilled Water Following Changes in Solutions of Different p_H*

p_H	Original Volume, Cc.	Volume Change After 18 Hours in p_H Solution, Cc.	Volume Change After 18 Hours in Distilled Water (After 18 Hours in p_H Solution), Cc.
2.0.....	4.45 3.85	-0.65 -0.8	-0.25 -0.05
2.85.....	3.6 4.35	-0.35 -0.25	+0.35 -0.4
3.9.....	4.7 4.8	+0.45 +0.4	-0.4 -0.65
4.8.....	4.25 3.2	+0.3 +0.3	+0.15 +0.05
5.8.....	5.05 4.9	+0.45 +0.25	-0.15 +0.35
6.85.....	4.35 4.5	+0.25 +0.25	+1.1 +0.65
8.15.....	4.45 5.3	+0.2 +0.25	+0.5 +0.0
9.6.....	4.35 4.3	+0.4 +0.65	+4.05 +3.55
10.6.....	4.45 4.65	+1.35 +1.65	+0.6 +1.9

ever, that the decrease in volume of pieces of vitreous in solution of different p_H was permanent. In the following series of experiments with the protected preparations described, the reversibility of such volume changes was studied by transferring the preparations after eighteen hours from the solutions of different p_H to distilled water. The figures of table 1 are in general consistent with Goedbloed's findings and prove that the volume changes are not reversible, especially in strongly acid (p_H 2) and alkaline (p_H 9.6 and 10.6) solutions.⁵ This behavior of the vitreous is different from that of hydrogels.

5. The only exception occurred in a solution of p_H 3.9 in which the gain in volume was regularly followed by an equal loss. No explanation can be given for this result.

Baurmann⁶ and Duke-Elder assumed that the ultramicroscopic picture of the vitreous is proof of its gel nature and compared it to that of some soap gels. Goedbloed drew attention to the fact that most hydrogels have no ultramicroscopic structure whatever, while the transitory one of soap gels cannot be compared to that of the vitreous. Goedbloed's criticism is valid insofar as it is directed at the identification of fibrils as micelles and vitreous fluid as intermicellary fluid. But it is not valid, as the following investigations will show, insofar as it denies other qualities of the vitreous which are characteristic of hydrogels.

Because of the definite expansion of the vitreous preparations in our experiments (in contrast to the loss found by other authors), it is feasible to compare this expansion with that of hydrogels. For a better understanding of this comparison some of the basic qualities of gels are reviewed. Although there are extremely different explanations of the nature of volume changes in hydrogels, there is little disagreement about the influence of certain outside factors on the capillarelectric charge and hydration of the substrate. The micelles of a hydrogel are thought to be in contact with each other at cohesion points; the free parts of the surface of these elements carry the hydration and capillarelectric charge. The intensity of the electric charge or the hydration may be changed from without, causing variations in dimension which are characterized by measurable differences in the volume of the gel. The absence or decrease of capillarelectric charge and the decrease in hydration may disturb the balance between contraction—and expansion—factors in such a way that forces of cohesion prevail. The gel structure will then contract until a new balance is reached. These changes in dimension are reversible principally if the number of cohesion points remains the same. The gel system will revert to its original volume if the primary charge and hydration are restored; the volume will increase if the hydration exceeds its initial stage. This concept of the micellar structure of gels and of its swelling and shrinkage, based on the work of Kruyt and his school, is followed here to simplify the complicated problem for ophthalmologists.

EXPERIMENTS WITH HIGH CONCENTRATIONS OF NEUTRAL SALTS

The first systematic study of the influence of neutral salts on colloid systems was carried out by F. Hofmeister. Different salts produce varying degrees of turgescence in gels and act differently in high and in low concentrations. A characteristic sequence of neutral salts in high con-

6. Baurmann, M.: Untersuchungen über die Struktur des Glaskörpers bei Säugetieren, *Arch. f. Ophth.* **111**:352, 1923; Untersuchungen über die Eigenschaften des Glaskörpers des Tierauges, *ibid.* **114**:276, 1924.

centrations is called by Freundlich the lyotrope series. These salts produce the swelling and shrinkage of gels by hydration and dehydration. Goedbloed examined the effect of such salts on pieces of cattle vitreous with the ultramicroscope and made the important observation that vitreous fibrillae showed sharper contours with dehydrating salts and more blurred contours with hydrating ones. He expressed the opinion

TABLE 2.—*Volume Changes in High Concentrations of Neutral Salts*

Salt	Concentration	Original Volume of Vitreous, Cc.	Volume After 24 Hours in Salt Solution, Cc.	Volume Change, Percentage
KCNs.....	0.25 N	4.2	4.8	+14.32
		4.95	5.25	+ 6.05
	0.5 N	4.7	5.8	+23.4
		3.95	4.8	+24.05
	1.0 N	3.8	4.5	+18.63
		4.3	5.05	+17.44
KI.....	0.25 N	4.3	5.0	+16.25
		5.3	5.35	+ 0.97
	0.5 N	4.0	4.95	+23.75
		4.76	5.6	+17.65
	1.0 N	4.45	5.65	+26.9
		4.8	6.0	+25.0
KNO ₃	0.25 N	4.05	4.1	+ 1.23
		5.1	5.35	+ 4.9
	0.5 N	4.0	4.5	+12.5
		4.05	4.3	+ 6.17
	1.0 N	4.8	5.3	+10.41
		3.9	4.35	+11.53
KCl.....	0.25 N	4.9	5.25	+ 7.5
		4.83	5.15	+ 6.62
	0.5 N	4.3	4.1	— 4.65
		3.9	3.7	— 5.13
	1.0 N	4.3	3.9	— 9.3
		4.45	3.9	—12.35
KF.....	0.25 N	5.35	5.25	— 1.86
		4.75	4.6	— 3.16
	0.5 N	4.15	3.6	—13.25
		4.1	3.5	—14.63
	1.0 N	4.15	3.5	—15.66
		3.85	3.4	—11.68
K ₂ SO ₄	0.25 N	4.7	4.45	— 5.31
		5.0	4.7	— 6.2
	0.5 N	4.48	3.5	—21.87
		4.35	3.4	—21.83
	1.0 N	5.2	3.95	—24.03
		5.18	4.2	—18.72

that these structural differences demonstrate actual hydration and dehydration of the fibrils, but he could not find any relation between the structural alterations and volume changes, and, what is more, the vitreous decreased in volume when strongly hydrating salts were used. Similar results were obtained by Baurmann with high concentrations of these salts and in our experiments when the vitreous preparations were without protecting membranes or without the nerve head. The results were different, however, when protected vitreous preparations were used, as in the following experiments.

Potassium salts in equimolar concentrations of 0.25, 0.5 and 1 normal were the selected neutral electrolytes, as they were employed by Bungenberg de Jong and Hennemann⁷ in experiments on agar and gelatin. The vitreous preparations went into colloidal solution somewhat (peptization) in the normal solutions of potassium rhodanide and potassium iodide. The figures for the volume at this concentration are therefore not accurate. In general the volume changes were characteristically constant, corresponding to the lyotrope series. The vitreous preparations swelled in solutions of potassium rhodanide, potassium iodide and potassium nitrate, increasing with the concentration. They shrank in 0.25 normal solutions of potassium fluoride and potassium sulfate, and

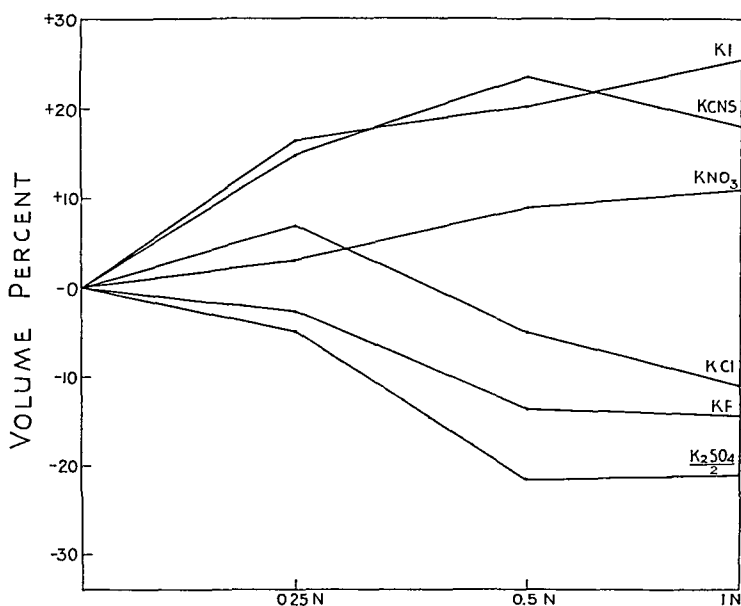


Chart 1.—Volume changes in high concentrations of neutral salts.

the shrinkage also was more pronounced in higher concentrations. They increased somewhat in volume in the weaker (0.25 normal) solutions of potassium chloride but decreased in higher concentrations. The sequence is therefore $\text{CNS, I} > \text{NO}_3 > \text{Cl} > \text{F, SO}_4$.

Chart 1 shows the varying amounts of the described volume changes. Chart 2 gives the results of experiments with gelatin reported by Bungenberg de Jong and Hennemann.⁷ The similarity of the two curves is evident. The nature of these variations in volume is explained by the hydration of the micelles, a theory which is widely accepted. The ultra-microscopic observations of Goedbloed confirm this view in the special

7. Bungenberg de Jong, H. G.: Zur Kenntnis der lyophilen Kolloide, *Kolloid-Beihefte* **29**:454, 1929. Bungenberg de Jong, H. G., and Hennemann, J. P.: Zur Kenntnis der lyophilen Kolloide, *ibid.* **36**:124, 1932.

case of the colloidal system of the vitreous. The action of electric charge plays no recognizable role in such concentrations of neutral salts.

The changes of volume in this series of experiments were reversible, like those of hydrogels in regard to shrinkage due to dehydration as well as in regard to expansion due to hydration. The vitreous preparations were measured after being removed from the normal solutions and were placed into 0.01 normal solutions of the respective salts. After twenty-four hours volume changes in the inverse direction were noted in all preparations. The initial volume was generally not restored, because

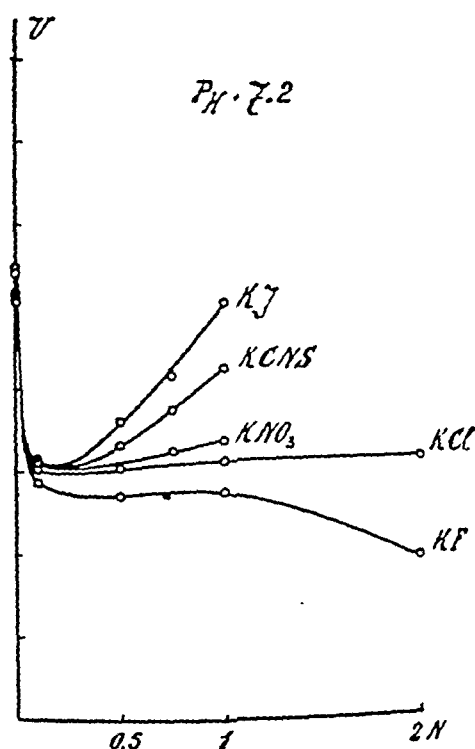


Chart 2.—Volume changes of gelatin in high concentrations of neutral salts. (From Bungenberg de Jong and Hennemann.⁷)

of irregularities in the extent of the oppositely directed volume shifts as shown by the figures of table 3. These can be explained by structural differences in the original preparations. Irreversible changes may be of some relevance, especially in the most marked volume gains in solutions of potassium iodide and potassium rhodanide. Such exceptions are likewise known in experiments with hydrogels and are supposed to be caused by far reaching lesions in the structure of the gel as prestages of peptization.

These experiments prove therefore that solutions of neutral salts in high concentrations cause marked reversible changes in the volume of vitreous preparations by their hydrating and dehydrating action. The

volume changes resemble to a great extent those of gelatin, following the lyotrope series of anions.

EXPERIMENTS WITH LOW CONCENTRATIONS OF NEUTRAL SALTS

Electrolytes in low concentrations cause shrinkage of gels. This shrinkage is supposed to be a capillarelectric process, a discharge phenomenon. The amount of shrinkage depends on the valence of the ion whose charge is opposite that of the gel. In a negatively charged colloid system, as, for instance, in the vitreous at a physiologic p_H , the shrinkage depends on the valence of the cation. The nature of the cation and the nature and valence of the anion are without influence on the shrink-

TABLE 3.—*Volume Changes in 0.01 Normal Solutions of Neutral Salts Following Changes in Concentrated Solutions of the Respective Salts*

Salt	Concentration	Volume Change in Concentrated Solution (After 18 Hours), Cc.	Volume Change in 0.01 N Solution (After 18 Hours) Following Change in Concentrated Solution, Cc.
KCNS.....	1.0 N	+0.55	—0.2
		+0.6	—0.35
	0.5 N	+0.53	—0.63
		+0.45	—1.05
KI.....	1.0 N	+0.6	—1.65
		+0.65	—1.6
KNO ₃	1.0 N	+0.25	—0.4
		+0.23	—0.9
KCl.....	1.0 N	—0.5	+0.25
		—0.28	+0.1
KF.....	1.0 N	—0.85	+1.0
		—0.85	+0.4
K ₂ SO ₄	0.5 N	—1.49	+1.82
		—1.45	+1.95

age (Schulze-Hardy law). It could be expected, therefore, that the action of the cations of electrolytes in low concentrations might interfere with the turgescence of the vitreous. The expansion of vitreous preparations in solutions of electrolytes of small concentration is vigorous. The counteractive effect of the salts could not be clearly demonstrated, mostly because of the difference in the original substrates, which resulted in different degrees of swelling, even, for example, in distilled water; only identical substrates could show small variations reliably. The technic was modified therefore in the following way. Desalination of the vitreous preparations by suspending them in flowing distilled water for twenty-four hours resulted in a 10 to 30 per cent swelling, due partly to the increased capillarelectric activity of the protein framework. The desalination was probably not complete, but this procedure could not be continued for forty-eight or seventy-two hours because of the disintegra-

TABLE 4.—*Volume Changes of Desalinated Vitreous Preparations in Low Concentrations of Neutral Salts**

Salt	Concentration, MEq.	Average Volume After Desalination, Cc.	Average Volume After Period in Salt Solution, Cc.	Average Change in Volume, Percentage
KCl.....	5	5.34	4.78	—11.07
	10	5.24	4.65	—11.13
BaCl ₂	5	5.47	4.62	—15.6
	10	5.55	4.68	—15.65
CaCl ₂	5	5.37	4.58	—15.3
	10	5.92	5.05	—15.4
Co(NH ₃) ₆ Cl ₃	5	5.52	4.57	—17.12
	10	5.27	4.33	—18.22

* The figures of this table represent the average of 3 experiments. The detailed figures of single experiments are available on request.

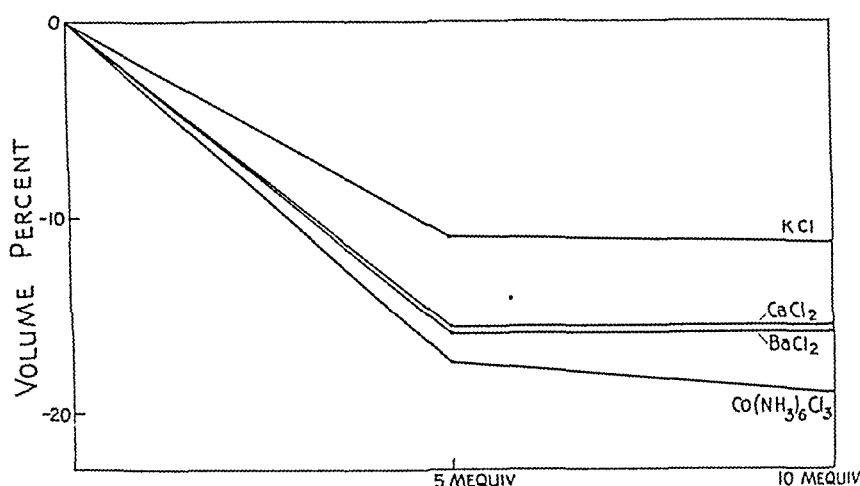


Chart 3.—Volume changes in low concentrations of neutral salts after desalination in distilled water.

tion of the covering structures. Preparations with about the same degree of swelling in distilled water were used for further investigations. After volumetric measurement they were put in solutions of monovalent, bivalent and trivalent chloride salts, respectively potassium chloride, barium chloride and calcium chloride, and hexamine cobalt chloride. Dilutions of 5 and 10 milliequivalents were used. After twenty-four hours all preparations showed a shrinkage, which was least in potassium chloride solutions and most in solutions of hexamine cobalt chloride. Barium chloride and calcium chloride solutions produced a similar shrinkage, the degree lying between that produced by monovalent and that produced by trivalent salts. Because there was the same volume decrease in equimolar concentrations of calcium chloride and barium chloride, the law which states that the nature of the cation has no effect on shrinkage in negatively charged colloid systems can be applied to the vitreous.

As shown in these experiments, changes can be produced in the volume of the vitreous by means of either factor, hydration or electric charge. In this respect the vitreous in toto acts like a real hydrogel.

EXPERIMENTS WITH ALCOHOL AS A NONELECTROLYTE

The influence of alcohol on the vitreous was studied as an example of the action of a nonelectrolyte. A decrease in volume occurred when the concentration of alcohol exceeded 40 per cent. The shrinkage increased with the increasing concentration of the alcohol. Chart 4 shows that the vitreous preparations lost about 30 per cent of their original volume in absolute alcohol. This loss was reversible. When the shrunken

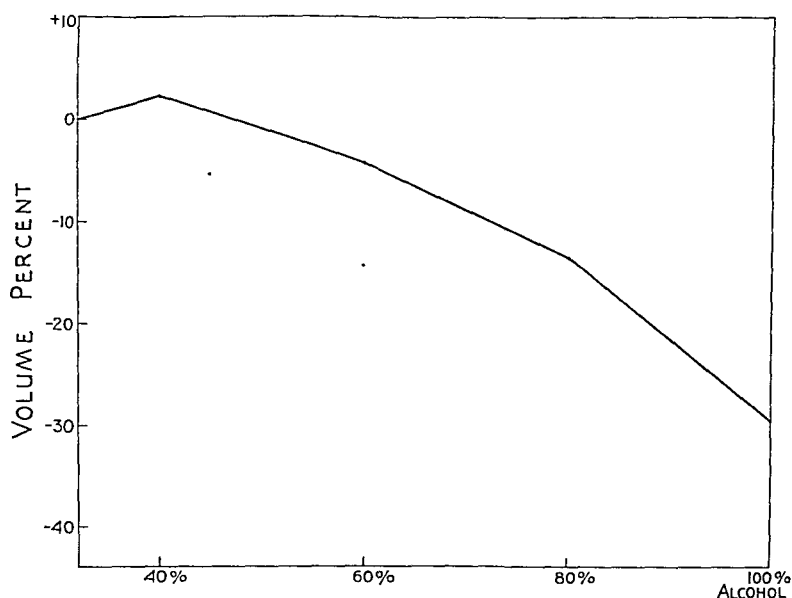


Chart 4.—Volume changes in alcohol.

TABLE 5.—*Volume Changes in Alcohol*

Alcohol	Original Volume of Vitreous, Cc.	Volume After 24 Hours in Alcohol, Cc.	Average Change, Percentage	Volume After Period in Distilled Water, Cc.
40 per cent.....	5.0	5.1	+2.28
	3.8	3.9		
60 per cent.....	4.55	4.38	-4.68
	3.55	3.35		
80 per cent.....	4.0	3.5	-13.7	4.65
	4.25	3.7		
Absolute alcohol.....	4.7	3.22	-29.7	5.15
	5.0	3.6		

vitreous was transferred into distilled water, the increase, owing to desalination, exceeded the original loss. As in gelatin gels, the decrease in volume can be explained by the dehydration of the micelles. Gelatin shrinks markedly, however, in 40 per cent alcohol and shows a greater decrease than that observed in the vitreous in alcohol of higher concentrations.

EXPANSION AND EXPANSION PRESSURE

The expansion tendency found in a milieu of physiologic solution of sodium chloride leads to the question of the nature and amount of this expansion and the pressure exerted by it. The first two points were discussed briefly in a previous paper.¹ As a result of new experiments, a rediscussion of these questions is indicated. Two explanations for the swelling of the vitreous in Ringer's solution and in physiologic solution of sodium chloride were given, namely osmotic processes and a prior

TABLE 6.—*Volume Changes of Pigs' Vitreous in Slightly Hypertonic Solutions of Sodium Chloride*

Sodium Chloride, Percentage	Original Volume of Vitreous, Cc.	Volume After 24 Hours in NaCl, Cc.	Volume Gain, Percentage
1.0.....	5.2	5.5	5.75
	4.3	4.45	3.49
1.1.....	5.07	5.2	3.59
	4.85	4.85	0
1.2.....	5.55	5.65	1.8
	4.98	5.03	2.01

loss of fluid in preparation (assuming a certain elasticity of the vitreous). In addition to the explanation of possible differences in partial salt concentration, it is conceivable that 0.9 per cent solution of sodium chloride and Ringer's solution are not isotonic to pigs' vitreous. Furthermore, Sugita⁸ stated that the postmortem liquefaction of the vitreous causes an increased osmotic concentration.

In relation to the first explanation, the behavior of the vitreous in slightly hypertonic solutions of sodium chloride, that is in 1.0, 1.1 and 1.2 per cent solutions, was studied. A small expansion was generally evident, as table 6 shows. In solutions of still higher concentrations a loss in volume was found.

To determine whether there is an increase in the osmotic concentration of the vitreous in the usual time for one experiment, the freezing

8. Sugita, Y.: Weitere Untersuchungen über das Wesen der spontanen Netzhautblösung, speziell über die Physikochemie ihrer Entstehung, Arch. f. Ophth. 139:561, 1938.

point depression was measured with the Beckmann-Heidenhain apparatus.

The average freezing point depression of portions of vitreous fluid obtained by centrifugation was 0.557 to 0.57 C. These figures correspond to those found by Cohen, Kamner and Killian⁹ and others but are lower than that found by Sugita. The figures of Cohen and his associates and Jess¹⁰ were obtained for vitreous fluid, while Sugita apparently used solid vitreous. These figures do not of course represent the true osmotic concentration of the vitreous in the living eye, since no attempt was made to prevent contact with air.

In my experiments the freezing point of pigs' vitreous was determined in two ways. In the first series of experiments vitreous fluid was obtained by centrifuging the isolated vitreous. Evaporation of fluid was prevented insofar as possible. In the second series of experiments the isolated vitreous bodies were cut up with scissors just before each measurement.

TABLE 7.—*Freezing Point Depression of Vitreous Fluid and Cut Vitreous Body*

	Vitreous Fluid, C.	Cut Vitreous Body, C.
Fresh preparations.....	Δ 0.57	Δ 0.5375
After 20 hours.....	Δ 0.5625	Δ 0.5515
After 28 hours.....	Δ 0.569	Δ 0.5515

Measurements were made immediately after the vitreous was dissected and on other vitreous or vitreous fluid after twenty hours. In this period the vitreous bodies and fluid were kept in tightly corked bottles with a thymol crystal at room temperature. This arrangement was selected in accordance with the technic of volumetric measurements previously described.

The results of these experiments, as table 7 shows, are different from those reported by Sugita on beef eyes kept at 6 C. He found on the second day a freezing point depression of 0.7 C., in contrast to that of 0.62 C. on the first day. In our experiments with vitreous fluid no increase in the freezing point depression was noticed. The results on cut vitreous bodies were less consistent; in some experiments no increase in the freezing point depression was evident after four hours. After twenty-four hours, however, the average increase of the depression in the series was 0.0176 C. The deviation varied in single experiments,

9. Cohen, M.; Kamner, M., and Killian, J. A.: Comparative Chemical Studies of the Ocular Fluids, of Cerebrospinal Fluid and of the Blood, Tr. Am. Ophth. Soc. 25:284, 1927.

10. Jess, A.: Zur Chemie des normalen und des pathologisch veränderten Glaskörpers, Ber. ü. d. Versamml. d. deutsch. ophth. Gesellsch. 43:11, 1922.

and it is questionable whether conclusions should be drawn from experiments on cut vitreous. On the other hand, even if these figures are accepted as proof of an increase in the molar concentration of the vitreous after twenty hours, they are so low that they cannot account for the usual increase in volume after a few hours.

A third group of experiments was carried out, with vitreous fluid used as the surrounding milieu to exclude any osmotic effect except that discussed in the previous paragraph.¹¹ Vitreous fluid was prepared as in the former experiments and a thymol crystal added, and the vitreous with the retina, ciliary body and nerve head was suspended in it. Table 8 gives the results obtained and shows that the average increase measured 5.93 per cent, in comparison with an average increase of 7.94 per cent in a solution of 0.9 per cent sodium chloride.

When the results of these three groups of experiments are summarized, it is apparent that osmotic effects are not responsible for the

TABLE 8.—*Volume Changes of Preparations of Pigs' Vitreous in Vitreous Fluid and in a Solution of 0.9 per Cent Sodium Chloride*

Vitreous Preparations in Vitreous Fluid			Vitreous Preparations in a Solution of 0.9 per Cent NaCl		
Original Volume, Cc.	Volume After 20 Hours, Cc.	Change, Percentage	Original Volume, Cc.	Volume After 20 Hours, Cc.	Change, Percentage
4.15	4.65	+12.0	4.8	5.25	+ 9.35
5.02	5.35	+ 6.55	4.2	4.5	+ 7.14
5.7	6.05	+ 6.13	4.7	5.2	+10.6
6.07	5.93	— 2.3	4.87	5.15	+ 5.73
4.8	5.15	+ 7.27	5.8	6.2	+ 6.89
Average.....		+ 5.93			+ 7.94

expansion of the vitreous in this type of investigation. Therefore this expansion must be considered as a turgescence phenomenon. It is not possible to determine, however, whether the expansion exceeds the amount of fluid which may be lost by compression during the preparation of the vitreous.

In regard to the expansion pressure of the vitreous, the difficulties involved in obtaining information in vitro are obvious, since the methods used in the determination of the turgescence pressure of gels cannot be used for the vitreous substrate. The technic worked out by Goedbloed did not give reliable results, but his apparatus, an onkometer, used in a different way threw some light on the problem.

The onkometer consists of a dialyzing cylinder connected to a water manometer by an inverted U tube which is filled with paraffin oil. Vitreous—in these experiments the vitreous preparations—was placed in the dialysis cylinder and covered with oil. This part of the apparatus

11. This group of experiments was suggested by Dr. Jonas Friedenwald.

was suspended in a vessel with an outlet near the rim. It contained the outside fluid (distilled water, saline solution, etc.), which could be continuously changed by a connection with a reservoir without interfering with the surface level. The upper level of the vitreous mass, the outlet of the vessel containing the outer fluid, the level between the paraffin oil and water in a sphere-shaped widening of the glass tubing and the level of the water in the manometer were in alinement before the experiment started.

Goedbloed attempted to measure the turgescence pressure of the vitreous (pieces of cattle vitreous) using distilled water as the outside fluid and found a pressure of 34 mm. of water. He considered this figure not as an exact expression of the turgescence pressure but as the sum of expansion and osmotic pressures. The osmotic pressure may change with the disintegration of the protein substances, especially of the mucoprotein, according to Goedbloed, and cannot be distinguished from the expansion pressure. The knowledge of the expansion pressure against distilled water (less than 34 mm.) is of only theoretic value, particularly since the figure is so small.

The same difficulty of distinguishing expansion pressure from osmotic pressure was present in my experiments with salt solutions of different concentrations (0.3, 0.6 and 0.9 per cent) and distilled water with the addition of 0.002 per cent phenylmercuric acetate as a preservative. The maximal manometer reading for distilled water was 200 mm. of water after seventy-two hours; for a solution of 0.3 per cent sodium chloride, 95 mm. of water after twenty hours; for a solution of 0.6 per cent sodium chloride, 88 mm. of water after thirty-eight hours, and for a solution of 0.9 per cent sodium chloride, 33 mm. of water after twenty-four hours. These figures represent an average of 5 experiments for distilled water and a solution of 0.9 per cent sodium chloride and an average of 2 experiments for solutions of 0.3 and 0.6 per cent sodium chloride.

To study the relation between expansion pressure and outside pressure, the technic was changed in the following way. Ten vitreous preparations (about 43 cc.) in one group or separated into groups of five were measured in a large volumeter and then carefully placed in the dialysis cylinder. With two groups of five, the vitreous preparations in the lower half of the cylinder were separated from those in the upper half by a dialysis membrane disk. The outer fluid was a solution of 0.9 per cent sodium chloride. The manometer was read after eighteen hours. The preparations were then removed from the dialysis cylinder and the volume was measured as before, with the preparations in one or two groups. It was found that the vitreous preparations gained volume (0.7 per cent) against a pressure of 33 mm. of water (2.4 mm. of

mercury). This increase in volume could be observed only in the preparations in the upper half. The pressure reduced the volume of the vitreous in the lower half, which had to withstand the pressure of 33 mm. of water and that of the overlying vitreous preparations.

The volume increased more in the onkometer against a pressure three times as great (100 mm. of water) when distilled water was used as the outer fluid. In these experiments ten vitreous preparations in one group were used. No attempt was made to find the maximal pressure necessary to prevent the expansion of the preparations in distilled water, because of the limited practical value of such a determination.

The results of experiments with the Goedbloed apparatus cannot be fully evaluated because of the factors which may interfere with the outcome. For this reason another, less complicated, technic was applied in a new series of experiments. The advantages of the new method are

TABLE 9.—*Volume Changes of Preparations of Pigs' Vitreous in Vitreous Fluid and a Solution of 0.9 per Cent Sodium Chloride Under Pressure Produced by Different Weights*

Pressure Exerted, Gm.	After 3 Hours, Percentage		After 4 Hours, Percentage		
	A. In Vitreous Fluid	B. In 0.9% NaCl	A. In Vitreous Fluid	B. In 0.9% NaCl	
				(1) Laboratory	(2) S-H*
0.5	+11.2	+12.0
1.5	+ 4.57	+4.2	+ 4.9	+3.1	+ 0.78
2.5	+ 0.9	+2.1	— 2.2	—5.3	—10.6
3.5	—10.1	—0.35	—14.1	—8.3	—25.7

* Experiment performed in slaughter house on freshly enucleated eyes.

that several measurements of individual vitreous can be made and that the number of experiments is not limited by the requirement of many complicated instruments. Rings of plasticine of different weight were mounted on cardboard bases and coated with paraffin. The weight and the volume of the rings were determined and the actual pressure exerted in the fluid calculated. The outer fluids used in the experiments were a solution of 0.9 per cent sodium chloride and vitreous fluid. Table 9 shows the volume changes of the vitreous preparations in the two fluids with different weights and after various intervals.

Repeated experiments did not give absolutely consistent results. Differences in the condition of the single vitreous preparations (time after slaughter, pressure exerted in preparation, etc.) may explain the variations. In an attempt to avoid the difference in time after slaughter, experiments were performed in the slaughter house on eyes enucleated a few minutes before use.¹² Pressure was exerted on the vitreous prepa-

12. Adolf Gobel, Inc., permitted the performance of these experiments in their building.

rations for four hours in a solution of 0.9 per cent sodium chloride. Expansion occurred against weights equal to 14.7 mm. of water. In previous laboratory experiments an expansion was found in this solution against a pressure of 31 mm. of water exerted for four hours. In vitreous fluid, however, no expansion occurred against a pressure of more than 27 mm. of water after four hours.

There are many reasons for not relating these figures of experiments *in vitro* to conditions in the living eye, but it is certain that the expansion pressure of the vitreous is not negligible, in spite of the statements of Duke-Elder, Baurmann and Goedbloed, who found an expansion pressure of less than 1 mm. of water. This figure lies within the limits of error of their method, which is objectionable because of the serious injury to the vitreous.

ELASTICITY OF THE VITREOUS

Volume elasticity is one of the characteristics of a hydrogel and distinguishes it from a hydrophil sol. Thus the hydrogel in a certain time regains its volume after it has been diminished by pressure. If the pressure is too great, however, the reversibility of the volume change may be incomplete because of essential alterations in the gel structure. It has been shown by Robertson and Duke-Elder that the isolated residual protein which forms the fibrils of the vitreous has a high degree of elasticity, but it has been repeatedly denied, especially by Goedbloed, that the vitreous *in toto* possesses any elasticity. According to this author the vitreous cannot regain its fluid content, lost by pressure, in a milieu in which the concentration of electrolytes equals that of the aqueous humor. But, in my opinion, this is true only if the balance of this heterogenic colloidal system is disturbed by the loss of capillary fluid at the injured base and area martegiani.

The following experiments were carried out with the onkometer of Goedbloed. Ten vitreous preparations, mostly divided into two equal groups, were measured and placed in the dialysis cylinder. In experiments with groups of five the technic was the same as that previously described. Pressure was exerted by filling the manometer tube to 150 mm. with water, which was a difference in level of approximately 200 mm. from the preparations in the lower half of the cylinder. Continually flowing solution of 0.9 per cent sodium chloride with 0.002 per cent phenylmercuric acetate as a preservative was used as an outside fluid. The water column in the manometer was refilled after the level had dropped from the 150 mm. maximum to 120 mm. The volume of the vitreous was measured after twenty-four hours, and the decrease was noted. The preparations were then kept floating in vessels with solution of 0.9 per cent sodium chloride. After twenty-four hours the

volume was again measured. The preparations which had been exposed to a pressure of 150 to 120 mm. of water and had lost 8.6 per cent of their original volume not only regained that volume but increased approximately 1 per cent beyond it. The preparations in the lower half, which lost 11.2 per cent, regained 7.2 per cent of their original volume.

Similar results were obtained in experiments with a simpler technic, as table 10 shows. Measured vitreous preparations were placed in small dishes filled with solution of 0.9 per cent sodium chloride, and weights of plasticine were put on them to produce different degrees of compression. After the volume was remeasured, the preparations were floated freely in continually flowing solution of 0.9 per cent sodium chloride for sixteen hours. Then they were remeasured.

It can be concluded from these experiments that pigs' vitreous preparations with a protected base and area martegiani may regain their

TABLE 10.—*Regain of Volume Lost by Pressure in a Solution of 0.9 per Cent Sodium Chloride*

Loss in Volume Caused by Pressure		Actual Increase in Volume When Pressure Was Released, Cc.
Percentage Loss	Actual Loss, Cc.	
3.42	0.18	0.78
4.32	0.2	0.85
5.0	0.2	0.23
6.18	0.3	0.75
6.25	0.35	0.35
9.0	0.44	0.4
9.9	0.48	0.4
27.9	1.1	0.25
32.3	1.5	0.25

initial volume, lost by pressure, as long as the pressure applied is not too great and the loss of fluid not more than 10 per cent. If the loss of fluid is more than 10 per cent, only a certain amount (7 to 8 per cent) of the loss will be regained. The vitreous body in toto possesses therefore elasticity in vitro.

COMMENT

The mechanism of volume changes of the vitreous is one of the basic problems in the physiology and pathology of the eye because of the possible relation to changes in tension of the eye and to certain displacements of intraocular structures. Such volume changes are the expression of the intake and output of fluid. The water-binding power of the vitreous may play an important role in the complexity of regulating factors and may determine the state of turgescence, deturgescence and turgescence pressure. Experiments on the vitreous in vitro are not expected to augment the knowledge of the circulation of vitreous fluid, its origin, regeneration and escape, but they may help to clarify the connection of water binding to volume changes.

The understanding of this relation could be more easily achieved if a classification of the colloidal structure of the vitreous and its definition as a histologic entity were unanimously accepted. As long as histologists and embryologists, clinicians and chemists, fail to agree on the nature of the vitreous as related to their respective fields, the experimenter on even one phase is confronted with difficulties.

The investigations reported here are allied mainly to the physico-chemistry of the vitreous, a field in which there is a divergence of opinions, as represented by the recent work of Baurmann, Duke-Elder and Goedbloed. Although one need not enter the dispute on terminology as to whether the concept of a gel should be confined to the definition of a hydrogel as given by Wolfgang Ostwald or should encompass a wider scope, some of the other points in dispute should be mentioned. The divergence on the interpretation of the p_H volume curve of the vitreous has been discussed. Goedbloed's standpoint that the volume changes of the vitreous in strongly acid and alkaline ranges cannot be compared to those of hydrogels was confirmed by the experiments with protected vitreous preparations in buffered solutions. The volume changes in solutions of different p_H (with one unexplained exception) were not reversible.

Goedbloed's objections to the definition of the vitreous in toto as a hydrogel, based on its ultramicroscopic structure, is sound. The vitreous fibrils should be considered as aggregates of micelles and not as the elementary unit of the gel, while the capillary-bound vitreous fluid may be compared to a hydrosol.

The investigations reported in this paper did not deal with separated constituents of the vitreous but were confined to the behavior of the vitreous in toto. In this connection some of the statements and conclusions of Goedbloed are of interest and are therefore summarized:

1. The vitreous volume decreases continuously in a solution of 0.9 per cent sodium chloride and does not show any expansion of its framework in solutions containing more than 10 milliequivalents of sodium chloride (0.0585 per cent). Therefore it lacks the qualities of a hydrogel under physiologic conditions.

2. Neutral salts with a strong hydrating effect cause an increase in the hydration of the vitreous fibrils; salts with the opposite effect cause a diminution; both effects are recognizable with the ultramicroscope.

3. Strong hydration of the fibrils does not result in an increase in volume; in fact, the volume decreases.

4. In a physiologic milieu the vitreous does not regain fluid lost by pressure when the pressure is released, and therefore the vitreous in toto possesses no elasticity.

5. The vitreous increases in volume in distilled water or in salt solutions of less than 10 milliequivalents exclusively by the increase in the electric charge of the fibrils.

In contradiction to the first statement, it was demonstrated in a previous paper that the vitreous did expand under approximately physiologic conditions, and recent experiments showed that the vitreous expands also in solutions of 1.0, 1.1 and 1.2 per cent sodium chloride, but to a lesser degree. A similar expansion was found when the preparations were kept in vitreous fluid. The volume increase is therefore a turgescence phenomenon and not the result of osmotic processes.

In other series of experiments on the vitreous in toto a number of qualities of hydrogels, denied by Goedbloed, were revealed: Reversible volume changes were produced by means of both expansion factors of hydrogels, i. e., by hydration and by the influence of electric charge. It was also found that after the pressure which had been applied was discontinued, the vitreous regained its volume (if the loss was less than 10 per cent) in a solution of 0.9 per cent sodium chloride. The vitreous in toto is elastic therefore to a certain degree. Finally, the existence of a turgescence pressure in physiologic solution of sodium chloride could be proved and the pressure approximately measured.

The volume changes of the vitreous by hydration and dehydration in solutions of neutral salts proved in a convincing way the applicability of a method which prevented the uncontrolled escape of capillary fluid. When the interrelation of the vitreous constituents and the architecture of the fibrils was not greatly disturbed, as in the vitreous preparations used, it was possible to achieve a better understanding of volume changes and their mechanism, of turgescence pressure and of elasticity.

CONCLUSIONS

1. The marked volume changes of the vitreous in strongly alkaline and acid ranges are not reversible. This finding verified the results of Goedbloed's experiments by means of another technic. The p_H curve of the vitreous is different therefore from that of a hydrogel.

2. The expansion of the vitreous observed in Ringer's solution and a solution of 0.9 per cent sodium chloride is not a result of osmotic processes, since it occurs also with vitreous fluid as the surrounding milieu. Nor is the expansion a result of increased molecular concentration due to postmortem decomposition, as determinations of the freezing point showed.

3. Hydrating and dehydrating neutral salts in high concentrations act on the vitreous as on gelatin. The effect of these salts on the volume follows the lyotrope series of anions.

4. The shrinkage and the swelling of the vitreous produced by these salts are reversible.

5. The vitreous shrinks by dehydration in concentrations of more than 40 per cent alcohol. This shrinkage is reversible, as in hydrogels.

6. At a physiologic p_H (p_H 7) desalinated vitreous shrinks in low concentrations of neutral salts. The degree of this shrinkage increases with the valence of the cation.

7. The vitreous in a solution of 0.9 per cent sodium chloride may regain the volume lost by pressure; therefore as a whole it is elastic to some degree.

8. The vitreous preparations expand in a solution of 0.9 per cent sodium chloride against a pressure of 31 mm. of water exerted for four hours.

Miss J. Di Grandi assisted throughout this study.

TUMORS OF CONJUNCTIVA AND LIDS

A BRIEF REVIEW

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Intraocular and intraorbital tumors comprise what may be called the concealed tumors of the organs of vision, that is those that may exist for a long time without being discovered and even after discovery may offer great difficulty in examination and in diagnosis.

On the other hand, tumors of the conjunctiva and of the lids, of the more important types of which this paper aims to be a concise but by no means a comprehensive review, may be called the revealed tumors of the organs of vision, for they spring from surfaces so exposed that morbid processes in them may be plainly seen by the naked eye. Their progress can be closely watched and the action on them of remedies followed.

TUMORS OF THE CONJUNCTIVA

Tumors of the conjunctiva are not unlike those found in mucous membranes in other parts of the body, although they have special significance on account of their proximity to the important organ of vision.

For the sake of convenience it is customary to divide tumors in general into two main groups, one being designated as benign and the other as malignant. A benign tumor of itself does not necessarily involve danger to life, whereas a malignant tumor if left alone will in the end prove fatal.

A. Benign Tumors of the Conjunctiva.—1. Simple Granuloma: The simple granuloma is probably the most common of the benign tumors of the conjunctiva. It is familiar as a soft-pediced mass often encountered on the surface of an incompletely closed tenotomy wound. It is particularly common in chalazions that have broken through the conjunctiva and have not been thoroughly dealt with. Sometimes, when the pedicle becomes very attenuated, the mass is brushed off by the motion of the lids. It is richly supplied with thin-walled blood vessels, so that it bleeds easily, and it is ordinarily the cause of the phenomenon of "blood tears." Granulation tissue may accumulate around a foreign body long embedded in the conjunctiva, as an attempt on the part of nature to render an irritant inert. It may attain great size and be so compressed

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by the action of the lids as to protrude, in the form of a thin purplish sheet, into the palpebral fissure and be mistaken for a sarcoma.

The treatment consists in excision, after which the granuloma seldom returns.

2. Polyp: By polyp of the conjunctiva one understands a smooth, pedicled translucent growth and above all else a growth covered by epithelium. It originates mostly in the fornix, its presence there usually being discovered by accident when the lid is everted. Occasionally it is large enough to protrude between the lids, showing a tendency to grow forward, as do all tumors of the conjunctiva. In its nature the polyp is a small fibrous overgrowth which pushes the conjunctiva before it. When it is large it is not unusual for its epithelial covering to be broken down by ulcers, so that it bleeds freely and in this way simulates granulation tissue. Indeed, Elschnig taught that no genuine polyp of the conjunctiva exists but that what is commonly termed a polyp is in reality a mass of granulation tissue which, as a result of the movements of the lids, has assumed a polypoid form.

The direction of least resistance in the conjunctiva is outward; hence all tumors, the sarcoma and the dermoid tumor as well, may assume a polypoid form.

The treatment, as with the granuloma, is surgical removal.

3. Papilloma: As the name indicates, the papilloma is a tumor in which the epithelial cells cover frail finger-like processes. It is especially distinguished from the polyp by a surface which is not smooth but nodular, like that of a raspberry or of a cauliflower. It has a core of fibrous tissue and blood vessels, which by division and subdivision may form a complicated mass. It usually originates in hypertrophy of mucous papillae. The bulbar conjunctiva contains no papillae; it is therefore not the usual field for the papilloma. The papilloma is found at the limbus, where there are papillae, or at the inner canthus in connection with the caruncle and the plica semilunaris. It may have a broad base and grow as a flat uneven layer over a large area of the conjunctiva.

It is asserted that at times the papilloma becomes malignant. For this reason, and because it has a well known tendency to recur, it should be thoroughly removed as soon as it is diagnosed. Some surgeons recommend curetting the base after excision and then using the actual cautery.

4. Angioma: The angioma is a benign tumor in the sense that after extirpation it does not recur and does not produce metastasis. Two principal forms are met with in the conjunctiva, namely the hemangioma and the lymphangioma.

(a) A hemangioma in the conjunctiva is rare. Histologically the hemangioma is a tumor consisting of blood vessels bound together by

a small amount of connective tissue. It is usually found in connection with the caruncle. The last one that I saw was in the bulbar conjunctiva on the nasal side of the cornea in the eye of a young girl. It appeared as a dark, purplish red, slightly elevated area some 8 mm. in diameter. It was increasing in size and was disfiguring. A few months ago it was excised and the adjoining conjunctiva was drawn over the defect. There has been no recurrence.

Because of the danger of hemorrhage in removing a large hemangioma, one method of removing the growth is first to tie it off by passing a straight needle bearing a double-armed suture through the middle of the base, cutting the suture at the needle and tying one thread around one half of the base and the other around the other half.

(b) The term lymphangioma refers especially to the small translucent beadlike dilatations of lymph spaces not infrequently seen in office practice in the bulbar conjunctiva. The dilatations are freely movable. They are commonly the result of friction, such as that produced when a patient is in the habit of closing his lids and rubbing them in response to a sensation of itching. They tend to increase in size and in number. They may even assume a polypoid form and appear between the lids. They are easily excised, but unless the eye is kept bandaged for a number of days afterward they are likely to recur. I have seen them disappear after mere bandaging of the eye.

5. Cyst: In the retrotarsal fold there occur retention cysts, which originate in Krause's glands because of occlusion of their excretory ducts. A large epibulbar cyst lined by epithelium may develop as the result of invagination of the conjunctiva, particularly after an operation on the muscles. It may become almost as large as the globe itself. One cyst has been reported that started from an operation at the limbus and in the end almost surrounded the globe as far back as the optic nerve.

The removal of a large cyst is accomplished by puncturing the anterior wall with a sharp knife and then excising a portion of it with forceps and scissors. The remaining wall is curetted and swabbed with tincture of iodine. By this method, sometimes followed by nature, as when the wall becomes necrotic from extension and bursts, the cavity formerly occupied by the tumor contracts and heals.

6. Lipoma: The subconjunctival lipoma is a firm, painless tumor generally situated on the upper and outer circumference of the eyeball. It is triangular, its sharply defined base lying toward the cornea. Although congenital, sometimes it grows to considerable size, so that it may become visible between the lids. If not removed it may undergo necrotic changes. One gets the impression in observing a subconjunctival lipoma over many years that it has traveled a little by sinking

lower on the globe, exhibiting the phenomenon of "gravity wandering" sometimes seen in the subcutaneous lipoma.

In the surgical treatment of the lipoma one point is worthy of emphasis. In removing any fatty subconjunctival tumor, whether congenital or acquired, it is wise not to follow it beyond the folds of transmission, leaving the deeper parts undisturbed. Especially in dealing with a subconjunctival congenital lipoma one should be careful not to excise any of the normal orbital fat with which it is apt to be connected posteriorly.

7. Dermoid Tumor: One of the commonest tumors of the conjunctiva is the dermoid tumor, a lenticular growth of solid consistency. It is always of congenital origin and arises as a result of cutaneous inclusion. This tumor, of varying size, usually straddles the margin of the cornea, with which it is immovably connected. It is sometimes confounded with the dermoid cyst of the orbit, but the latter is a hollow formation and not a solid one, as is the dermoid tumor. Descriptions of dermoid tumors appeared in the literature as early as 1742. Occasionally such a tumor attains considerable size at puberty, and it may cause irritation when hairs grow out from the surface.

If remnants are left when a dermoid tumor is excised, the tumor may in part form again. However, no attempt should be made to dissect the tumor down to clear corneal tissue, since it usually extends into the deeper corneal lamellae and an attempt at such thorough removal may result in perforation. It is to be expected that the site of the tumor on the cornea will remain clouded permanently.

8. Nevus: The nevus of the conjunctiva, like a nevus, or mole, elsewhere on the body, represents an anomaly of development. Although benign, it possesses a distinct capacity to become malignant. Its site of predilection is in the bulbar conjunctiva close to the cornea, in the field where the pinguecula, pterygium, papilloma, epithelioma and sarcoma are apt to develop. In its commonest form it is a small, slightly elevated brownish or even blackish lesion. The darker the spot the more prone it is, so it is thought, to become malignant.

No tumor of the conjunctiva requires more careful attention than a nevus at the limbus. When it shows the slightest sign of spreading or of deeper pigmentation, and especially of enlargement of the blood vessels that supply it, it should be surgically removed. It is essentially a tumor in the conjunctiva and is freely movable with it. The danger border is at the corneal margin where the conjunctiva is intimately adherent to the sclera. In the dissection an attempt should be made to include the anterior layers of the sclera and of the cornea.

B. *Malignant Tumors of the Conjunctiva.*—Epibulbar malignant tumors are in reality conjunctival in origin. They almost never arise

from the cornea. As to their nature and their malignancy, they follow the same law as do tumors of embryonic origin arising in other tissues of the body. There are two epibulbar tumors that warrant principal attention—the epibulbar sarcoma and the epibulbar carcinoma. They occur mostly in elderly patients, but youth does not exclude their presence.

1. *Epibulbar Sarcoma*: The base of the epibulbar sarcoma is in most instances small, even though the tumor itself may overlap a considerable area of the cornea and appear to spring from it. It differs from the general sarcoma with regard to malignancy only so far as it is isolated on the highly resistant cornea and sclera and is visible practically from the start. It usually comes to operation early. Unless it is far advanced it seldom penetrates into the interior of the eye. Its site of predilection is the limbus.

In every case, once the clinical diagnosis is confirmed by microscopic examination enucleation of the globe to which it is attached should be advised, provided the fellow eye has serviceable vision.

2. *Precancerous Melanosis and Diffuse Malignant Melanoma of the Conjunctiva*: In 1938 Reese¹ reported the clinical and pathologic observations in 8 cases of acquired pigmentary changes in the conjunctiva, which he termed precancerous melanosis. He pointed out that such changes may be the precursors of a diffuse malignant melanoma. He expressed the opinion that this tumor arises primarily from the potentially pigment-bearing basal layer of the conjunctiva.

Turning to the relation of acquired melanosis to the nevus, I find that it serves my purpose to quote from Reese's paper: "A nevus of the conjunctiva is not an obligatory precancerous lesion, whereas an acquired melanosis ultimately becomes malignant." According to Reese's experience many more malignant melanomas of the conjunctiva arise from an acquired melanosis, or spontaneously, than from a nevus. He stressed the fact that congenital melanosis of the conjunctiva, as seen in highly pigmented races and in melanosis oculi, is not to be confounded with acquired precancerous melanosis.

As to treatment, it was Reese's advice that nothing short of early exenteration of the orbit should be attempted, and he recommended that immediately after the exenteration the walls of the orbit be lined with a Thiersch graft in order to save many weeks of dressings.

3. *Epibulbar Carcinoma*: All parts of the conjunctiva are not equally liable to be affected by carcinoma. However, as with sarcoma, the site of preference is the limbus and most often the outer side. The carcinoma may remain for a long time confined to the superficial layers of the con-

1. Reese, A. B.: Precancerous Melanosis and Diffuse Malignant Melanoma of the Cornea, *Arch. Ophth.* **19**:354-365 (March) 1938.

junctiva and of the cornea. Its extension into the superficial layers of the cornea simulates the pannus of trachoma or of keratoconjunctivitis eczematosa. The tumor conforms to no set rule, as it may remain stationary for a long time at about the size of a pea or may all at once take on a rapid exuberant growth, attain an enormous size and in the end project into the palpebral fissure as a fungating mass. It may extend widely over the sclera and in rare cases slowly and steadily surround the cornea, in which case it is known as a peribulbar epithelioma. It is not likely to have well defined margins, as does a typical sarcoma. Penetration into the globe is rare but is more likely to occur than with the sarcoma. The epibulbar epithelioma is said to be more often a transplantation from the lids than a primary growth.

The danger of local recurrence and of metastasis being less than with the sarcoma, a less radical form of treatment is indicated. In suitable cases, when the tumor is small and appears to penetrate no deeper than the movable conjunctiva it may be excised after the method of the excision of a nevus. In other cases, in which it is evident that the deeper layers of the cornea and of the sclera are implicated, enucleation is indispensable if the fellow eye has serviceable vision.

C. Tumors of the Lids.—Of all the tumors of the lids, both benign and malignant, the sarcoma and the carcinoma are the two of prime importance.

As to the fibrous tarsal plate of the lid, the greater portion of its bulk is tunneled out to accommodate glandular structures. Malignant growths in these glands do occur, yet they are so rare and so often not correctly diagnosed that most clinicians will never see one.

1. Sarcoma: The sarcoma may arise from any structure of the lids except the epithelium. A flat pigmented congenital nevus in the intermarginal space is considered, like a nevus at the limbus, to be particularly dangerous for the development of melanotic sarcoma. Care should be taken not to molest a nevus of the lid when the lid is being treated for any purpose.

The primary sarcoma of the lid makes its appearance as a rounded, usually slightly reddened nodule under the skin, fairly well circumscribed. In the early stages it may simulate the chalazion, but it is not always located over the tarsus and the skin may not be freely movable over it. The tendency is to rapid growth, the abundant blood supply favoring this. Ulceration and invasion of the orbit proceed together. Glandular involvement is the rule, the glands in front of the ear enlarging first and those along the jaw and in the neck later.

The earliest possible removal of the tumor is imperative, but in spite of the removal of the tumor from its bed and the immediate use of radium, local recurrence and metastasis are to be feared.

2. Carcinoma: Carcinoma of the lids occurs oftener than sarcoma. In dealing with a carcinoma one's chief concern is with the skin immediately surrounding the palpebral border. Dermatologists emphasize the fact that in the case of a carcinoma of the skin the age of the patient is not so important as the evident age of the skin involved.

There are two varieties of carcinomas of the lids, namely the squamous cell carcinoma and the basal cell carcinoma (Jacob's ulcer, rodent ulcer). The latter tends to remain very superficial and is the less malignant of the two. With each when typically developed there is little tumefaction in the strict sense of the word but there is an ulcer with an uneven floor and an irregular hard waxy wall. As the carcinoma advances on one side it shows deceptive signs of healing on the opposite side.

Because ulceration predominates, an inexperienced observer may readily mistake the true nature of a carcinoma of the lids, which is nothing else than a cancerous process. Its progress is proverbially slow and painless, often prolonged over many years. However, it must be noted that when the ulceration affects the infraorbital or supraorbital nerves or the bony wall of the orbit it may cause the most excruciating pain.

Histologically, a point of interest is the condition of the connective tissue stroma between the down-grown plugs of epithelium. Cancerous epithelial cells seem to exert an irritating influence on preexisting tissue, which responds by a productive inflammatory reaction causing scirrhus. This inflammatory reaction is absent in the case of benign growths, such as the papilloma, the lipoma and the angioma.

RELATION BETWEEN TUMORS OF THE LID AND INTRAOCULAR TUMORS

A definite relation has been brought to light between malignant tumors of the lids and intraocular melanomas of the uvea. Thus, Gardner² in 1940 published the clinical and pathologic observations in a case in which von Recklinghausen's neurofibromatosis of the lids and a melanoma of the choroid were present at the same time. He found 3 similar cases reported in the literature.

HANDLING OF TUMORS

In studying a growth suspected to be malignant one should be careful to handle the tissues gently. The habit today is to take specimens for biopsy carelessly and indiscriminately. A specimen should be taken only when it is imperative to confirm a diagnosis. At all times one should be mindful of how easy it is to disseminate malignant cells into the field adjoining the tumor.

2. Gardner, S.: Malignant Melanoma of the Choroid and von Recklinghausen's Disease, *Am. J. Ophth.* **23**:73-78 (Jan.) 1940.

TREATMENT

Before attempting any form of treatment for a malignant growth one should seek the opinion of a specialist in tumors. Under no circumstance is the use of any form of caustic or cautery or of curetting to be recommended. Such treatment is painful and far less sure than the use of radium. When a carcinoma is relatively small and superficial, according to my experience, treatment by roentgen rays and radium gives the most satisfactory results. This is the treatment for basal cell carcinoma that Dr. Ewing used to recommend to his students at Cornell. He explained that the cells are distinctly radiosensitive and may be destroyed with a minimum amount of damage to surrounding tissues. He emphasized that the success of this treatment is due to the fact that there are a great number of capillaries in carcinomas and that these are readily destroyed by radiation. Moreover, radiation sterilizes the tissues in a wide area around the visible, palpable tumor. Unfortunately, in the carrying out of this treatment the majority of patients are inadequately treated, so that recurrences follow because of insufficient doses. Once a tumor of the lids has penetrated to the orbital tissues or has involved the bone it is hard to irradiate it with the right dose. Under these circumstances one is compelled, as John Hunter said, to lay down science and take up the knife.

CAUSES OF BLINDNESS IN PENNSYLVANIA

AN ANALYSIS OF THE BLINDNESS IN OVER THIRTY THOUSAND EYES

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Since the enactment in Pennsylvania, in 1934, of legislation granting pensions to blind persons, a great number of eligible and ineligible persons have made applications for these pensions. The result is that at present we are able to analyze and tabulate the causes of blindness in the 31,352 eyes of 15,676 persons 21 years of age or over whose visual acuity was 20/200 (6/60) or less and who were therefore considered industrially blind. This is according to the definition of blindness as adopted by the Committee on Statistics of the Blind.¹

At the end of the first year of the administration of the act for granting pensions for blindness a report was made based on an analysis of the causes of blindness in 11,852 eyes. This report was read before the Section on Ophthalmology of the American Medical Association in Kansas City, Mo., on May 13, 1936.²

On Oct. 6, 1936 a second report,³ based on a total of 18,193 eyes, was read before the Section on Eye, Ear, Nose and Throat of the Medical Society of the State of Pennsylvania. This, therefore, is the third analysis. It is based on the ophthalmologic reports on all applicants as of Jan. 1, 1941 and includes the statistics in the two previous papers.

Read before the Section on Ophthalmology at the Ninety-Second Annual Session of the American Medical Association, Cleveland, June 4, 1941.

1. A body composed of representatives of the American Foundation for the Blind, the National Society for the Prevention of Blindness, the American Association of Workers for the Blind and the Statistical Committee of the Section on Ophthalmology of the American Medical Association.

2. Cowan, A., and Sinclair, S. M.: Causes of Blindness in Pennsylvania, from the Medical and Social Aspects, *J. A. M. A.* **107**:757-759 (Sept. 5) 1936.

3. Cowan, A., and English, B. C.: Distribution of Blindness in Pennsylvania, *Pennsylvania M. J.* **40**:180-184 (Dec.) 1936.

As far as we can ascertain, this is the greatest number of blind eyes included in a single report up to this time. Since the information from which the analysis was made was obtained in every instance by an accredited ophthalmologist, we feel that with respect to both the given causes and the etiologic factors it is as dependable as can be expected in a study of this kind. A critical reader will notice certain discrepancies between the number of cases in the smaller groups of this series and the number in such groups in the series previously reported. The explanation is that in many instances pensioners were reexamined for various reasons and a different diagnosis was sometimes made by another examiner or even by the same examiner. On the whole, however, these discrepancies are so comparatively few that they can be considered as of little consequence. Again, we might be criticized for not having used the classification set up by the Committee on Statistics of the Blind.

We realize that there is a definite advantage in using a universal method of recording causes and etiologic factors of blindness, and we should have been only too glad to use the classification of the Committee on Statistics of the Blind, but we could not with any satisfaction do so. Such factors as "myopia, other refractive errors—specified," "refractive errors not specified" and "motor anomalies" are never causes of blindness. Many terms are too vague, and many of the causes named are secondary and not primary. For example, "hypertension (glaucoma)" is given as a cause. Hypertension secondary to uveitis, as a heading, is given as a primary cause. We feel that hypertension secondary to uveitis should be designated as a cause of blindness no more than should macula of the cornea as a sequence of interstitial keratitis. Symptoms and sequences are too frequently given instead of disease entities as the actual cause of blindness. Such terms as "pannus," "vascularization of the cornea," "phthisis bulbi" and "atrophy of the globe" refer to sequences and should not be used as headings under which causes of blindness can be listed in a report of this kind.

Another criticism we offer is that there are too many terms for the same condition. For example "iritis," "iridocyclitis," "uveitis" and "keratoiritis" might all be classified under "uveitis." Again, under choroid and retina there appear such headings as "retinitis," "chorio-retinitis," "retinal hemorrhage" and "arteriosclerosis of choroid and retina." Furthermore, we feel that in a report of this kind it would be superfluous to classify the blindness due to traumatism as having been "acquired during play or sport," "while performing household duties" or "in traffic." This type of breakdown is of value only to one who is particularly interested in such matters.

TABLE 1.—*Causes of Blindness*

	No. of Eyes		No. of Eyes
Congenital anomalies		Disease of cornea	
Glaucoma.....	168	Dystrophy.....	36
Defect of globe *.....	812	Keratitis, interstitial (1.1%).....	339
Albinism.....	10	Keratitis from exposure.....	3
Anophthalmos.....	15	Keratitis, ulcerative (1.4%).....	448
Neuroretinitis.....	2	Keratitis rosacea.....	2
Coloboma of choroid.....	7	Keratitis, phlyctenular.....	32
Cataract.....	443	Keratitis disciformis.....	2
Atrophy of optic nerve.....	168	Keratomalacia.....	6
Coloboma of optic nerve head.....	2	Keratoconus.....	27
Amblyopia.....	4	Keratitis of undetermined cause.....	70
Anomaly of optic tracts and centers.....	1		
Total (5.2%).....	1,632	Total.....	965
Trauma or traumatism		Disease of uvea	
Penetrating wound of globe †.....	1,559	Uveitis (11.9%)‡.....	3,746
Uveitis.....	238	Choroiditis.....	1,387
Sympathetic ophthalmia.....	381	Staphyloma of choroid.....	2
Keratitis.....	192	Total.....	5,135
Insect bite of globe.....	11	Disease of lens	
Chemical burn of globe.....	233	Cataract, senile (28.8%)§.....	9,032
Hemorrhage into vitreous.....	14	Cataract, diabetic.....	25
Rupture of choroid.....	9	Cataract from tetany.....	2
Cataract.....	168	Cataract from endocrine dysfunction.....	2
Detachment of retina.....	43	Cataract, presenile.....	60
Atrophy of optic nerve.....	294	Total.....	9,121
Disease of optic tracts and centers...	13	Disease of retina	
Neuroretinitis.....	37	Detachment.....	189
Photophthalmia.....	2	Macular degeneration.....	323
Total (10.3%).....	3,224	Retinitis, vascular (5.06%) 	1,589
Disease of lids		Retinitis, diabetic.....	576
Carcinoma.....	6	Retinitis, nephritic.....	41
Entropion.....	6	Retinitis pigmentosa (1.8%).....	570
Total.....	12	Total.....	3,283
Disease of conjunctiva		Disturbance of vitreous humor	
Diphtheritic conjunctivitis.....	2	Hemorrhage into vitreous.....	20
Gonorrheal conjunctivitis.....	39	Disease of optic nerve	
Ophthalmia neonatorum (2.4%).....	768	Atrophy (7.7%).....	2,402
Purulent conjunctivitis.....	73	Neuroretinitis (2.3%)¶.....	714
Pemphigus.....	22	Papilledema.....	164
Pterygium.....	21	Total.....	3,280
Trachoma.....	163	Disease of optic tracts and centers.....	44
Total.....	1,111	Miscellaneous	
Disease of globe		Amblyopia.....	21
Glaucoma, chronic } 11% {.....	3,297	Amaurosis.....	4
Glaucoma, acute }.....	162	Nystagmus.....	2
Glaucoma, juvenile.....	9	Total.....	27
Tumor of globe.....	17	Grand total.....	31,352
Exophthalmos.....	9		
Total.....	3,494		

* Includes all congenital defects of the globe which could not be specifically classified.

† Includes wounds due to foreign bodies within the eye, adherent leukoma, gunshot wounds, injuries from explosions and injuries vaguely described.

‡ Includes conditions diagnosed as iritis, iridocyclitis, keratoiritis, plastic iritis, cyclitis and complicated cataract.

§ All diabetic cataracts that occurred in persons over 50 were considered senile.

|| Includes all nontraumatic intraocular lesions due primarily to vascular disease, such as hemorrhages and exudates in the retina, embolism, thrombosis, retinitis proliferans and angiosclerosis.

¶ Includes all conditions diagnosed as retinochoroiditis, choriorretinitis, optic neuritis, etc., which resulted in atrophy of the optic nerve and also conditions designated as secondary optic atrophy or optic neuritis without other notation.

In table 1 the classification is arranged under twelve headings, as in the two previous reports. This classification is used again because we believe that it sets forth in the fewest possible terms and with clarity and simplicity the causes of blindness and will be understood by the ophthalmologist, the social worker and the intelligent layman. The table was compiled from the ophthalmologic reports on 15,676 blind persons, but because in so many instances the cause of blindness was different for the two eyes of one person the diagnosis for each eye was tabulated, and the supervising ophthalmologist chose from each report only the primary disease, the condition which he considered to be the main cause of blindness. He felt privileged, also, because of the great number of reports by so many ophthalmologists, to modify and condense many of the terms used.

The incidence of a few outstanding causes of blindness as shown by this report and the incidence as shown by the two previous reports are compared in table 2.

TABLE 2.—*Outstanding Causes of Blindness in the Three Reports*

	First Report, Percentage	Second Report, Percentage	Third Report, Percentage
Ophthalmia neonatorum.....	3.9	3.2	2.4
Congenital anomalies.....	4.5	4.7	5.2
Trauma.....	14.63	13.0	10.3
Glaucoma.....	13.34	12.9	11.0
Uveitis.....	12.6	13.4	11.9
Senile cataract.....	22.49	24.2	28.8

It will be noted from table 3 that a possible etiologic factor was reported for the blindness in 20,763 of the eyes. In many cases the information cannot be considered reliable, which is to be expected, since in nearly every instance it had to be obtained from the applicant himself. A glance at the list of etiologic factors in table 3 will convince any experienced ophthalmologist of the truth of our contention. As an outstanding example of how much value can be placed on such information, one may consider the naming of syphilis as an underlying cause of blindness. It is only reasonable to suppose that the blindness in more than 14 of the 513 eyes affected by an ulcerative or undetermined type of keratitis resulted from syphilis. There were 5,132 eyes in which the blindness was caused by uveitis or choroiditis, and in only 370 instances was syphilis given as a factor. Of 3,116 cases of simple atrophy of the optic nerve or neuroretinitis, syphilis was given as a factor in only 1,100. Of a total of 1,632 cases listed as instances of congenital anomalies, syphilis was given as a factor in none. Thus, if we add the 339 cases of interstitial keratitis to the cases in which blindness resulted from conditions

This procedure was inaugurated in May 1939, five years after the enactment of legislation granting pensions. As of January 1941, 7,057 ophthalmologic reports had been studied, and 25.4 per cent carried a definite recommendation for treatment which might result in restored or improved vision. The procedures recommended included extraction of cataract, treatment for glaucoma, treatment for systemic disease and refraction. Two methods of follow-up were employed: First, the applicant was referred to an agency engaged in the prevention of blindness; second, contact was established with the applicant through correspondence. The following tabulation is an analysis of the number and percentage of applicants dealt with by each method:

Total number of applicants.....	7,058	
Number for whom treatment was recommended	1,792	25.4%
Referral to agencies.....	779	43.4%
Contact through correspondence.....	1,013	56.5%

Persons referred to agencies for the prevention of blindness were visited by workers who interpreted the ophthalmic condition and explained the ophthalmologist's recommendation.

Of the applicants with whom contact was established through correspondence, 85.1 per cent replied to a letter asking whether the recommendation had been carried out and offering assistance if the applicant for some reason had not been able to seek medical care.

Of the 1,792 persons for whom an attempt was made to secure treatment, operations have been performed or scheduled for 11.1 per cent; treatment has been established for 12.8 per cent, and further contact is pending for 19.3 per cent. Of the remaining 57.6 per cent, some have rejected treatment, some have died and some present contraindications to surgical intervention. The fact that contraindications exist has been stated by the applicant and has not been verified by a physician.

In the follow-up of the 1,013 persons who could not be referred to a specialized agency we have experienced many problems. It was immediately recognized that it would be difficult through correspondence alone to assist applicants to understand their need for treatment and to help them make use of available resources. It is impossible in such a study as this to estimate accurately the value of the services rendered by the agencies for the prevention of blindness through direct contacts with the applicants. However, the percentage of persons for whom surgical and medical treatment was secured was higher among those referred to the agencies than among those reached through correspondence. It is interesting to note that only 3.3 per cent of the entire number were sufficiently resourceful to seek treatment for themselves.

One of the most difficult problems was the securing of adequate medical and surgical care for applicants living in rural sections in which there was neither an ophthalmologist nor a hospital equipped to give ophthalmologic service. Incidental to the program of urging persons to seek the recommended treatment, we have been able to establish three ophthalmic clinics, free hospital service in four institutions, the cooperation of ten ophthalmologists in giving medical and surgical treatment and the cooperation of county commissioners in six counties in supplying transportation, all in sections of the state where no ophthalmologic service had previously been available.

Since this effort has restored or improved the vision of 11.1 per cent of the persons with whom contact was established and has thereby resulted in a substantial saving to the commonwealth in payment of pensions, it would be an economically sound investment for the legislature of Pennsylvania and of other states with pension laws to appropriate funds for an adequate program for the restoration of vision and the prevention of unnecessary blindness.

ABSTRACT OF DISCUSSION

DR. C. W. RUTHERFORD, Indianapolis, State Supervising Ophthalmologist, Division of Blind Assistance, Indiana State Department of Public Welfare: I wish to outline causes of blindness as found in Indiana. The register of blind persons in Indiana on June 30, 1940 contained the names of 2,358 men and 1,914 women, a total of 4,272, or 125 per hundred thousand of population; it is not claimed that the register is complete. On December 31, 1,379 men and 1,046 women, a total of 2,425, or 71 per hundred thousand of population, were receiving from the Indiana State Department of Public Welfare monthly assistance checks because of blindness. Included in this group were 101 Negro men and 79 Negro women, a total of 180, which is 7.4 per cent of the 2,425 recipients, while for the entire state Negroes represent only about 3.5 per cent of the population. During the period 1934 to 1941, 238 children were enrolled in the Indiana State School for the Blind.

Indiana has but two sources for the organized study of causes of blindness, the department of public welfare and the state school for the blind. Both use the terminology of the standard classification of causes of blindness as published by the Committee on Statistics of the Blind. Figures for blind recipients and blind students cannot be combined because some of the latter are now included among the former. Eligibility for assistance because of blindness or for ophthalmic treatment in Indiana begins at the age of 21 for men and 18 for women.

Eligibility for monthly assistance based on visual acuity requires that the central vision of the better seeing eye with correcting lens be reduced to 20/200 or less or that no diameter of either visual field exceeds 20 degrees even though the central vision may be better than 20/200, e. g. as in retinitis pigmentosa. The school admits children whose central vision with correcting glasses is 20/200 or less.

When the causes of blindness are compared statistics are often deceptive for several reasons:

1. Data on blind persons who have been successfully treated are removed from tabulations. They should be retained but the case designated as inactive; otherwise their value for study is lost.

2. Most applicants for assistance because of blindness are first examined as to eligibility and causes of their blindness many years after the occurrence of the original disease or injury; unless secondary changes are recognized as such and distinguished from primary changes, and both are properly appraised, errors are sure to appear in the statistical study.

3. Medical records to establish eligibility for monthly assistance or ophthalmic treatment are at present executed by a state-wide staff of 115 approved medical graduates. Their preparation of records reflects their ophthalmologic training and experience, personal interest and cooperative spirit, and the value of a report is measurable by the same factors. The average examiner exhibits much more confidence in diagnosing a blinding condition than in determining its causation.

4. Undetected malingering adds confusion to statistics.

Because of more vigilant medical examinations, successful treatment and detection of malingering or exaggeration, there are now fewer recipients in Indiana of assistance because of blindness than there were three years ago.

The practical purpose of studying causes of blindness is the formulation of plans for restorative or stabilizing treatment, to conserve vision and to prevent blindness. Diagnosis teaches how the eye and visual functions are impaired or destroyed by conditions resulting from disease and trauma, but determination of the etiologic factor is of first importance because it indicates where attacks must be made to mitigate or eradicate the causes. Exposures to infections and injuries must be controlled.

DR. HARRY S. GRADLE, Chicago: The authors have given the first nearly accurate report on the causes of blindness. As it was compiled from the reports of a large number of ophthalmologists (certified, I hope) certain inaccuracies in terminology as well as in interpretation were bound to creep in, but they probably constitute a minor percentage.

Certain of the figures seem inexplicable. How does the state of Pennsylvania, with a total population of 9,891,000, have 15,676 applicants for the blindness pensions (approximately 13 per cent of the entire blind population of the United States), while Illinois, with a population of about 7,877,000, has 7,659 persons receiving blindness pensions and 823 additional applicants? This produces a ratio in Pennsylvania of 158 blind persons per hundred thousand of population; the similar figure for Illinois is 102 per hundred thousand. Within the next few years, when the ineligible have been weeded out of the pension rolls, the latter ratio will be reduced to less than 80 per hundred thousand. Evidently the question of ophthalmic care is not a deciding factor, for in Pennsylvania there are 148 ophthalmologists and in Illinois 134.

Merely for the sake of comparison, I have tabulated the percentual causes of blindness recorded by the authors and those found by Best in approximately 40,000 cases from the 1928 United States census:

	Cowan	Best
Congenital anomalies	5.2	4.0
Traumatism	10.3	16.5
Diseases of:		
Conjunctiva	3.5	5.2
Globe	11.5	5.4
Cornea	3.0	1.2
Uvea	16.3	0.7
Lens	30.0	13.7
Retina	10.4	1.6
Optic Nerve	10.4	6.9
Miscellaneous	2.6	44.8
	<hr/> 100.0	<hr/> 100.0

No survey, thorough as it may be, is of great value unless it is followed by an even more intensive corrective program. The latter must be compulsory if it is to be of real economic value and must be based on close cooperation between the examining ophthalmologist, the law-enforcing bodies and the various medical and surgical agencies employed in correction. The authors have proved this most conclusively in their closing pages and have presented definite percentual results that corroborate the shadowy figures at which some investigators have guessed. In Illinois a similar program of ophthalmologic analysis of the pension roll is being carried out, and while it is still too soon to present statistics, it has been found that about 25 per cent of the persons drawing \$1 a day from the state for their loss of sight should be removed from the rolls either because their vision is too good or because their defects can be remedied and useful vision restored. When more states follow the lead of Pennsylvania and employ their leading ophthalmologists to survey their blind population with the ultimate aim of a corrective program, then federal, state, local and lay agencies will be able to work more intelligently for the much more important task of the prevention of blindness.

His criticism of the type of detail under trauma might seem justifiable to ophthalmologists, but details of accidents are important to workers for the prevention of blindness.

These statements are made because the committee developed its classification with advice from ophthalmologists throughout this and other countries. It has been successfully used in a larger series than the Pennsylvania one.

Four courses are open to ophthalmologists: (1) Try Dr. Cowan's plan, accepting his interpretations; (2) let every one wishing to classify causes of blindness develop his own plan, with a return to chaos and a

loss of comparability and usefulness of the statistics; (3) attempt to use the much more complicated classification developed for another purpose by the National Conference on Nomenclature of Disease, even though members of that conference approve the shorter classification of causes of blindness, and (4) continue to use the classification of the Committee on Statistics of the Blind and work toward its further improvement. The committee hopes that Dr. Cowan will adopt the fourth plan and make his findings available for comparison with those from other states.

DR. CONRAD BERENS, New York: Members of the Committee on Statistics of the Blind regret that Dr. Cowan did not feel it advisable to follow the example of other states, which are using the committee's classification of causes of blindness. This classification has the approval of American ophthalmologists and of the Social Security Board for use in such studies and was being considered for international use.

Apparently Dr. Cowan has not seen the latest revision of the classification or the instructions for its use, as he has made errors of interpretation. For example, the instructions state that terms such as motor anomalies are acceptable only in classifying partially seeing persons, since the eyeball must be affected to cause blindness. The committee rejects sequelae as causes of blindness, accepting the term phthisic or atrophic globe only when the cause is undeterminable. Incidentally, how does Dr. Cowan classify these conditions, and is not pannus a factor in active trachoma, not merely a sequela?

He errs in assuming that the committee classifies secondary glaucoma or any other secondary condition as a cause.

He criticizes the length of the committee's classification. The committee might agree to further combinations but questions whether ophthalmologists would consider Dr. Cowan's combinations invariably sound. His list is actually longer than the committee's and reverts to the inconsistencies of older statistics.

DR. ALFRED COWAN, Philadelphia: We do not pretend that our classification is final. We merely believe that the classification as recommended by the Committee on Statistics of the Blind is not the right type for such a paper as this, the purpose of which is to inform ophthalmologists, social workers and interested laymen with regard to the primary causes of blindness.

When a person is hit in the eye, we want to know whether that person is blind, and the committee says that he was hit in the eye with a piece of stone. What is the difference? He was hit in the eye. If it is desired to classify traumatisms further, that is all right. We do not say that this should not be done if one is interested in the type of traumatism which causes blindness; we merely think that for purposes of a paper of this kind our way is all that is necessary.

I still contend that a scar of the cornea is not a primary cause of blindness; nor is pannus. I also contend that myopia is merely a consequence of some preexisting disease of the eyeball, usually uveitis. That of course is merely my opinion. Phthisis bulbi was mentioned. Is phthisis bulbi a primary disease? Every ophthalmologist knows that it is the end effect. It is a shrinking of the globe as a result of disease.

If an ophthalmologist examines a patient who is unintelligent and cannot give necessary information, we expect him to write in his report

that there is phthisis bulbi which is probably the result of uveitis, a penetrating wound or whatever he thinks the cause may have been, and we accept his opinion. There may be occasional errors, but how many will be found in a study of 16,000 blind persons? Too few to have an important effect on the final result.

Dr. Gradle wanted to know if senile cataract was the cause given for blindness before as well as after operation. I say this: Senile cataract is the primary cause of blindness whether or not the eye has been operated on. A person with senile cataract who has not been operated on is considered blind for the purpose of our paper and for the purpose of a pension. If a patient has been operated on, complications set in and blindness results, the original cause of blindness is considered to be senile cataract.

MODIFICATION OF THE BREWSTER STEREOSCOPE FOR CLINICAL REQUIREMENTS

EMANUEL KRIMSKY, M.D.

BROOKLYN

The familiar Brewster stereoscope consists of a rigid tubular type of viewing head that covers the eyes and much of the face. This viewing head contains a pair of lenses that are usually decentered outward so as to permit inspection of a pair of large stereoscope pictures, each 3 by 3 inches (7.6 by 7.6 cm.), which are pasted on a single card. The viewing distance can be changed, but to a rather limited extent. In the early part of this century the entertainment value of the stereoscope in providing illusions of a third dimension gradually faded. The subsequent adaptation of the stereoscope to clinical requirements consisted in replacement of the pictures by targets that could convey some meaning as to the fusion status of the eyes.

Because of the rigid nature of this simple instrument, the information that such targets could offer was suggestive rather than conclusive, qualitative rather than quantitative, and the training with the device that was prescribed was empiric, often of imaginary benefit and without regard for the patient's particular type of binocular dysfunction or for any preliminary understanding of what constitutes an average normal response with a stereoscope. It remained for Worth and his successors, who had modified the Wheatstone type of stereoscope, as exemplified in the amblyscope, to explore further the possibilities of that type of stereoscope for the measurement of fusion responses as well as of deviations.

The changes made in the Brewster stereoscope to provide for a certain flexibility in convergence as well as in divergence readings were few and consisted mainly of incorporating rotary prisms (Bielschowsky stereoscope) or graded prisms (Hazen kratometer) in the viewing head, without necessarily altering the fixity of the stereogram. In 1934, on the basis of calculations designed to show the effects on the positions and movements of the eyes of displacements of stereoscope targets, of varying interlenticular separations and of changing viewing distances, I designed a flexible experimental model to enable me to select the desirable features already incorporated in this type of instrument and

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to add features I considered clinically necessary. I felt that the Brewster stereoscope demanded the following improvements in order to compete with the Wheatstone type of stereoscope with regard to the changes already made in the latter for purposes of binocular investigation as a prerequisite to binocular training:

1. Sufficient elasticity to permit measurements of convergence and of divergence for different ranges of accommodation was made possible by separating, or decentering, the lenses and by the use of small medially decentered targets. Thus the amount of supplementary base-out prisms for added convergence could be reduced markedly to avoid undue chromatic aberration.

2. The instrument was calibrated to provide direct readings in terms of prism diopters for far and for near vision without needless computations. The prismatic value for each millimeter of lateral separation varies with the viewing distance, and one must calculate the amount of displacement in terms of prism diopters for each distance. However, a means was provided for making direct readings in terms of prism diopters for the two common testing ranges—the "O" and the 3 D. accommodation, respectively—by employing two rules automatically calibrated to compensate for such variations. For other ranges a reference table is all that the examiner requires (table).

*Prismatic Equivalent Chart for Selective Accommodations in Terms of Millimeter Displacement**

Accommodation, D.	Viewing Distance, Cm.	1Δ	5Δ	10Δ	1 Mm. 5 Mm. 10 Mm. Prism Diopters		
		Millimeters					
"O"	20	1	5	10	1	5	10
1	16.5	0.83	4.15	8.3	1.2	6	12
2	14	0.7	3.5	7	1.43	7.15	14.3
3	12.5	0.625	3.1	6.25	1.6	8	16
4	11	0.55	2.75	5.5	1.82	9.1	18.2
5	10	0.5	2.5	5	2	10	20
13	5.5	0.275	1.86	2.75	3.63	16.2	36.3

* The accommodation ranges are based on the use of ± 5 D. sph. viewing lenses.

The method of computation used in this table is as follows:

The displacement of an image by a 1 D. prism at a distance of 100 cm. amounts to 1 cm. (or 10 mm.). Such displacement by a target at that distance (as in the stereoscope) instead of by a prism would produce the same effect. In my phorometric stereoscope both targets move symmetrically, although the movable slide rule (beneath the right viewing box) indicates the readings for both eyes.

At the 20 cm. viewing distance in this stereoscope (or "O" accommodation for ± 5 D. sph. viewing lenses) 1 prism diopter would indicate a target displacement of 2 mm. or, if divided between the two eyes, of 1 mm. for each eye as indicated on the slide rule.

In the same way, at the 16.5 cm. viewing distance, which represents 6 D. of accommodation without viewing lenses but only 1 D. of accommodation with + 5 D. sph. viewing lenses, 1 prism diopter would mean $1:100::x:16.5$ (cm.), and x equals 1.65 mm., or an 0.83 mm. displacement on the slide rule for each prism diopter.

To obtain the prism value for each millimeter of the displacement on the rule, merely transpose or divide the aforementioned readings into 1.

The slide rule on the phorometric stereoscope is engraved on both surfaces; one surface is in millimeters, which provides direct readings in prism diopters for the "O" accommodation range only; the other surface is engraved to furnish direct readings in terms of prism diopters for the 3 D. accommodation testing range.

3. The instrument was made adjustable so as to enable the examiner readily to bring the targets in line with the primary positions for any selective accommodative ranges. For example, in order to bring the targets in line with the primary positions of the eyes for far vision, the instrument is set at the viewing distance corresponding to the focal length of the viewing lenses (or the "O" accommodation mark on the base rod) and the targets are adjusted to the "O" convergent position (fig. 2). By shortening the viewing distance to the 3 D. accommodative range the primary position of the targets is altered for that amount of accommodation. Such uniformity in the relation between accommodation and the primary position of the targets can be maintained as long as the interlenticular separation is fixed. In a previous model, which I built for research studies, the viewing head provided for a varying interlenticular separation as well as for the insertion of lenses of different strengths. Such an arrangement required a list of tables to show the different primary positions for the different lenses and interlenticular separations in relation to different viewing distances.

4. Convergence or divergence of the eyes for selective accommodative ranges was brought about by corresponding displacement of the targets in relation to the respective primary positions, rather than by the operation of graded prisms in the viewing head, in order to keep the viewing frame as free as possible for inspection of the patient's eyes. Target displacement proved more interesting to the patient, and calibrations could be seen more readily on his viewing the box than on his viewing the frame.

5. The clear visibility of the patient's eyes was made possible by freeing the viewing head from all unnecessary encumbrances, by the use of lenses of large diameter, by the incorporation of a reflecting mirror to enable the examiner to observe the eyes of the patient without exciting his suspicion and by the use of brightly illuminated transparencies, which could produce bright reflexes on the corneas (fig. 3).

6. Due provision was made for the insertion of various adapters; for example, calibrated adapters to provide vertical target displacement to either eye, an adapter to produce a graded stereoscopic effect for the

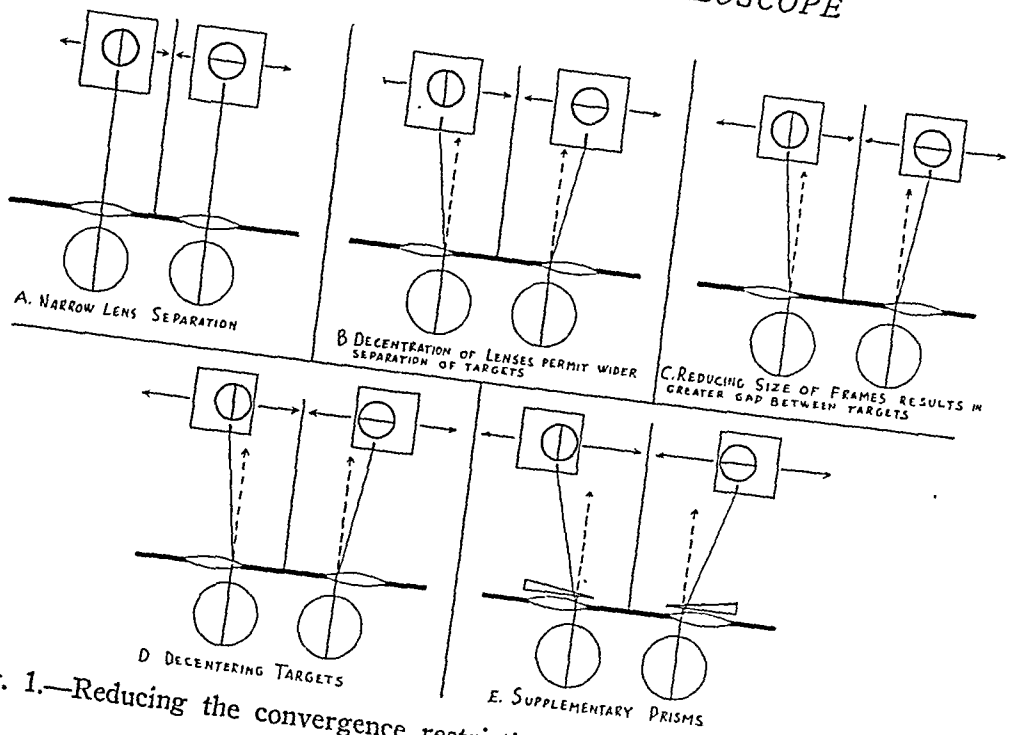


Fig. 1.—Reducing the convergence restriction of the Brewster stereoscope.

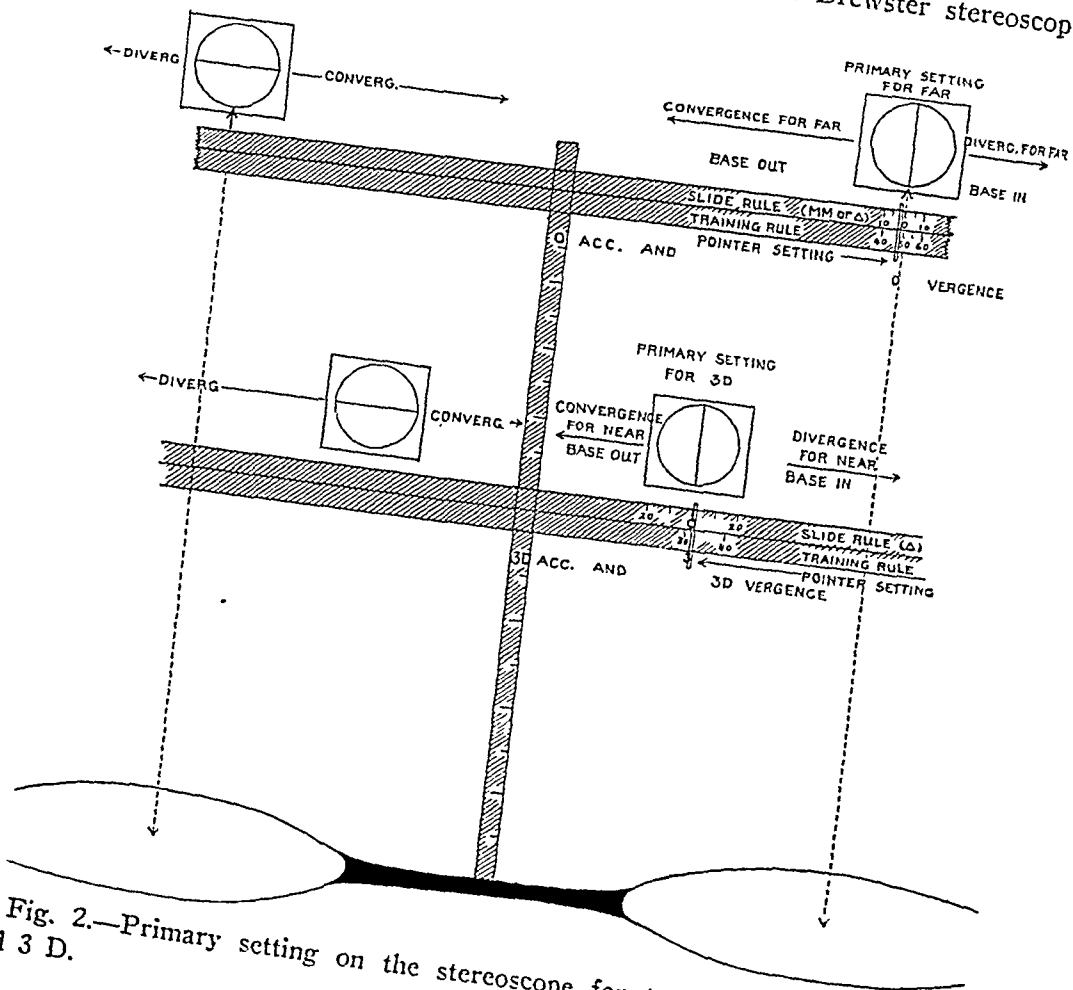


Fig. 2.—Primary setting on the stereoscope for two testing ranges—infinity and 3 D.

measurement of stereopsis and a reducing adapter to permit the ready insertion of 2 by 2 inch (5 by 5 cm.) kodachrome slides, glass plates or other transparencies for this common size.

7. Transparent and brightly illuminated targets were found to produce better illumination of eyes as well as brilliant corneal reflexes for purposes of objective study, and they also helped in the study of abnormal retinal correspondence as well as in cases of amblyopia. The targets were set in independent holders, or carriers, to permit their flexible separation or approximation; variation at will in the amount

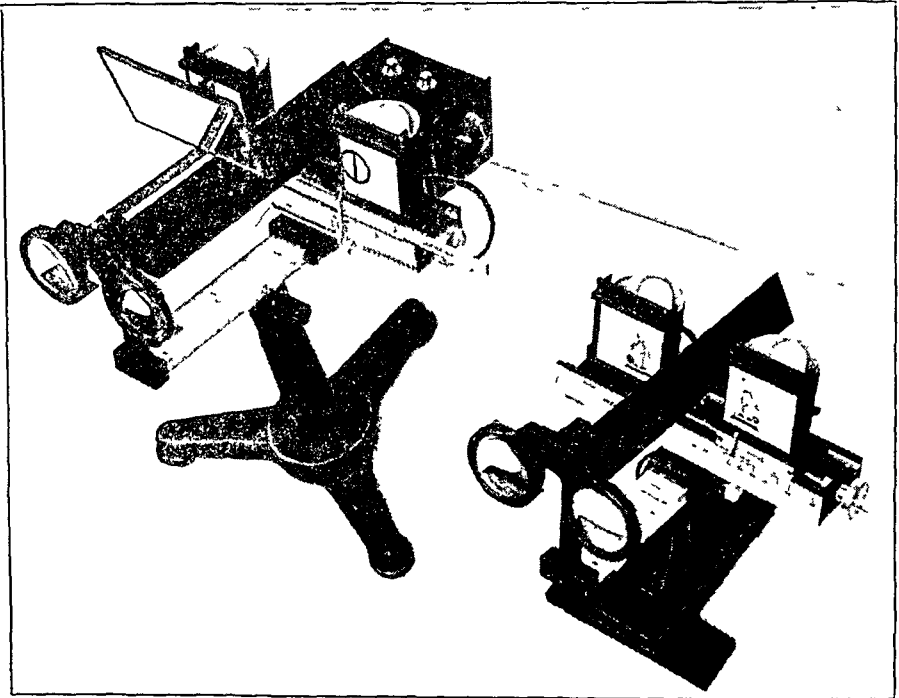


Fig. 3.—The diagnostic and the training stereoscopes (unretouched photograph).

of lighting to each eye was made possible by independent flashers. Displacement of targets was made symmetric rather than individual in the interests of simplicity of operation and of uniformity in readings. As in the case of prism testing, it mattered not whether target displacement was directed to one eye or equally to the two eyes. Displacement of targets was mechanical and its operation manual rather than automatic. In certain instances, especially in cases of true retinal correspondence, the manual operation of the instrument by the patient was found to yield a better vergence response than did passive operation. By active cooperation on the part of the patient there was brought about a stimulation of hand-eye movement, or so-called psychophysical parallelism. As simple an act as convergence was often found to be appreciably

greater when the patient was made to fix his eyes on his own finger rather than on that of the examiner.

The instrument was made simple and rigid, and the features of doubtful clinical value were carefully avoided, for example rotary movements of the targets. While there may be value in vergence with rotation of the eyes, it would appear logical that the breaking up of disjunctive imbalance in one direction of gaze would appear enough of an accomplishment without adding the conjugate factor of rotation of the eyes. The instrument does not provide for lateral rotation of the eyes in a locked vergence position, as does the synoptophore. While this feature

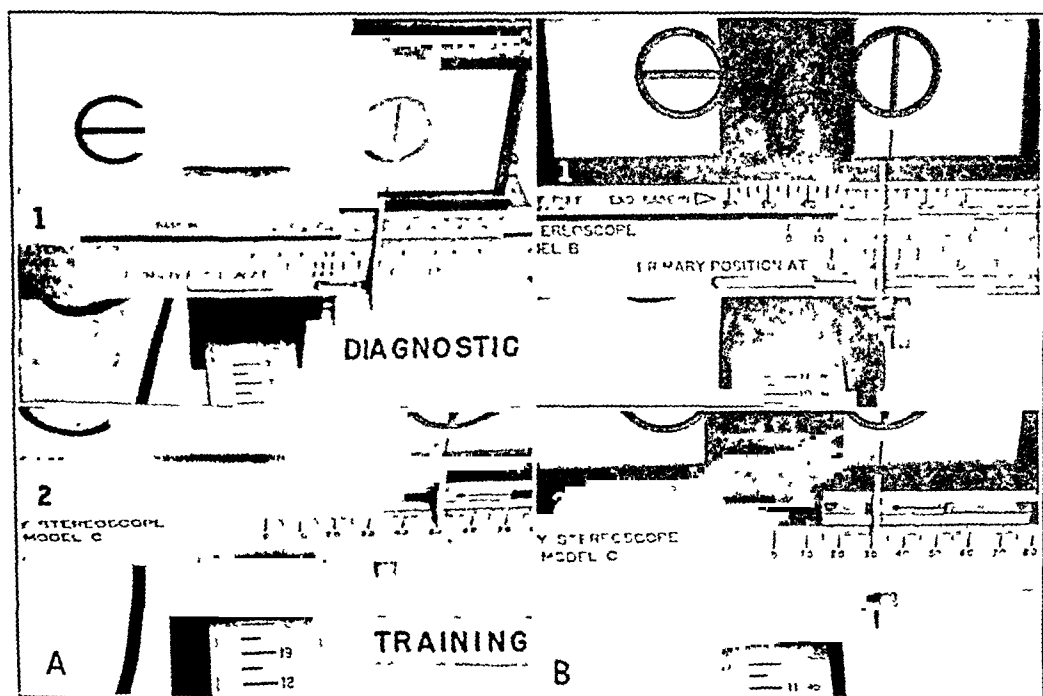


Fig. 4.—Primary settings on the diagnostic and the training stereoscopes. *A*, for infinity; 1, viewing distance 20 cm., or "O" accommodation on the base rod; 2, pointer setting at "O" diopter, or the 50 mm. mark, the same as on the diagnostic instrument above. *B*, for 3 D. accommodation: 1, viewing distance 12.5 cm., or 3 D. accommodation on the base rod; 2, pointer setting at 3 D., or the 31 mm. mark, the same as on the diagnostic instrument above.

may be easily incorporated in this type of instrument, it would also add to the details and problems involved in training.

As a diagnostic instrument, it was designed to measure as far as is possible in a comprehensive way binocular function in a manner parallel to that of screen and prism tests. It was intended to supplement rather than to replace the established screen test for purposes of confirmation and completeness and to provide added proof in evaluating the need for possible binocular training. As a training instrument it was designed

to provide prism training in a pleasant manner with due regard for the psychologic and clinical needs of the individual patient.

On the basis of both prism and stereoscope measurements, binocular dysfunction was classified according to the following accepted standard: divergence insufficiency and excess and convergence insufficiency and excess. Training was therefore prescribed in selected cases not merely to provide "base-in" or "base-out" exercises by operation of the instrument without regard for the particular range of the accommodative defect. By disregarding accurate settings of the instrument the examiner may think he is prescribing "base-out" training when as a matter of fact he is producing the opposite effect, as, for example, when setting the targets in relation to parallelism of the visual axis for a 3 D. accommodative range (fig. 2).

One of the vexing problems in the use of the stereoscope concerns the corrections to be made for changes in pupillary separation. This subject was clarified in a previous report which proved that pupillary separation can be disregarded in stereoscope readings and that the relation between variations in such pupillary separations and a fixed interlenticular separation serves automatically to compensate for any errors that might otherwise occur through the prismatic effects of relative decentration.¹

On the basis of consistent use, I find that for patients presenting varying degrees of deviation as well as binocular dysfunction one can carry out essentially the same studies with a calibrated Brewster type major stereoscope as with the major amblyoscope. Among these are studies of (a) abnormal retinal correspondence, (b) fusion amplitude (convergence and divergence; breaking and recovery points), (c) horizontal and vertical phorias, (d) vertical vergences, (e) amount of stereopsis and (f) macular or paramacular suppression.

In favor of the Wheatstone type of stereoscope is the greater flexibility in convergence range without the possibility of chromatic aberration. However, one can overcome the restriction of these factors in the Brewster stereoscope to a marked extent by the use of small decentered targets, decentered viewing lenses and only moderate strength of the added prisms when these are required. With a stereoscope having a 100 mm. interlenticular separation and with fairly small split targets, the eyes can be adapted to a convergence of at least 35 prism diopters for the infinity-equivalent range ("O" accommodation) and to at least 25 prism diopters of added convergence for 3 D. of accommodation

1. Krimsky, E.: The Stereoscope in Theory and Practice, *Brit. J. Ophth.* **21**:161-197 (April) 1937; Some Newer Developments in Precision Type Stereoscopes, *Arch. Ophth.* **19**:394-402 (March) 1938; Psychologic Considerations in the Study of Binocular Function, *ibid.* **21**:662-670 (April) 1939.

without resort to supplementary prisms. The addition of 40 prism diopters of base-out prisms (in the prism holder) is sufficient for the investigation of convergent squint in most cases, and the slight chromatic aberration is not enough to interfere with binocular investigation.

In cases of more extreme convergent squint binocular function is too impaired to provide positive information that may help one in diagnosis or in training. In such cases the measurement of deviation alone is the best that can be expected. From the standpoint of training one cannot hope for appreciable improvement with the stereoscope or with the synoptophore in cases of marked convergent squint. The milder types of convergent squint that are amenable to binocular training should therefore be as amenable to training with the Brewster type of instrument as with the Wheatstone type.

From the standpoint of training the major amblyoscope as constructed at present requires the physician or assistant to manipulate the light carriers. In the case of true projection much valuable time can be saved by entrusting to the patient the manipulation, or displacement, of targets for the required defect range. The patient can be made to cooperate actively rather than to remain a passive observer.

The Brewster type of stereoscope lends itself to ample selection of accommodative ranges. By shortening the viewing distance I can bring as much as 13 D. of accommodation into play without having to resort to compensating lenses, as with the Wheatstone stereoscope. The major Brewster stereoscope is designed to emulate the changes in positions of eyes for different accommodative ranges. While the position of the eyes in looking through a stereoscope both for an infinity-equivalent range and a 3 D. accommodative range may be the same as in ordinary vision for 20 feet (6 meters) or for 13 inches (33 cm.), respectively, the position of eyes in relation to targets is a flexible matter dependent on the strength of the viewing lenses, the interlenticular separation, the viewing distance and the incorporation of supplementary prisms.

OCULAR CONDITIONS ASSOCIATED WITH COLIFORM BACTERIA

CLINICAL AND EXPERIMENTAL OBSERVATIONS ON COLIFORM BACTERIA
INFECTIONS OF THE UPPER RESPIRATORY TRACT

CONRAD BERENS, M.D.

AND

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The pathogenicity for the rabbit of coliform bacteria isolated from the upper respiratory tract of man has been considered in previous investigations.¹ The present communication is concerned with the possible significance of these organisms in various acute and chronic ocular diseases in man. A large number of patients with serious uveal inflammation have been found to harbor coliform bacteria in their respiratory passages. Since these bacteria have been isolated from the same patients on repeated cultures, often in pure culture, they probably should not be considered transitory invaders. Moreover, it appears that an agent capable of producing a toxin as pathogenic for the rabbit as that produced by coliform bacteria might in man in the presence of sensitized tissues or lowered resistance produce severe acute or chronic ocular disease.

In view of these observations and of the apparent affinity of the toxins of these microbes for the uveal tissue of the rabbit, it seemed desirable to investigate their possible role in the causation of diseases of the eye of man. This report concerns the incidence of coliform bacteria in patients, the ocular diseases together with which they were found and the results of vaccine therapy. A careful analysis of the histories of the patients, a number of whom were observed for several years, may clarify the possible relation between the presence of coliform bacteria in the upper respiratory tract and the ocular and the systemic symptoms associated with them.

Aided by a grant from The Ophthalmological Foundation, Inc.

Read before the Section on Ophthalmology at the Ninety-Second Annual Session of the American Medical Association, Cleveland, June 5, 1941.

1. (a) Berens, C.: Nilson, E. L., and Chapman, G. H.: Iritis Produced in Rabbits' Eyes by the Intravenous Injection of Crude and Purified Cultures of Bacteria Isolated from Patients with Certain Inflammatory Eye Diseases, *Am. J. Ophth.* 19:1060, 1936. (b) Berens, C., and Nilson, E. L.: Experimental Acute Iridocyclitis in Rabbits Produced by Coliform Bacilli Isolated from the Upper Respiratory Tract of Man, *Tr. Am. Ophth. Soc.*, 1940, vol. 38.

Before the clinical observations are discussed, certain factors concerning some phases of experimental ocular lesions associated with infection due to coliform bacteria will be considered.

CLASSIFICATION OF COLIFORM BACTERIA

Although much work has been done in the attempt to classify the gram-negative organisms now grouped as coliform bacteria, the classification is still in a state of great confusion. This appears to be caused mainly by the marked instability of the biochemical properties of these bacteria,² which permits them to alter their characteristics from those of one species to those of another according to age, a shift in environment or factors not yet determined. In 1939 Parr² summarized the important findings concerning these organisms and concluded with the suggestion that for the present they be termed coliform bacteria.

TABLE 1.—*Comparison of Varieties of Coliform Bacteria Encountered in the Upper Respiratory Tract and in the Intestinal Tract in Man*

	Typical Esch. Coll, Percentage	Atypical Esch. Coll, K. Pneumoniae, Paracolon Bacilli, Proteus and B. Pyocyaneus, Percentage
Strains from upper respiratory tract (120).....	22.2	70.8
Fecal strains (125).....	62.0*	38.0

* These were isolated from patients with chronic diseases. The proportion of typical Esch. coll would undoubtedly be higher in persons having no symptoms of chronic disease.

Included in the group are the Klebsiella genus (the Friedländer bacillus), Aerobacter aerogenes, typical and atypical strains of Escherichia coli, Morgan and paracolon bacilli, Escherichia freundii, Shigella, Eberthella, Salmonella, Aerobacter cloacae and Proteus. Topley and Wilson³ stressed the difficulty of identifying the different members of this group by ordinary laboratory methods, especially in distinguishing between the A. aerogenes and Klebsiella pneumoniae groups, which many workers believe to be identical. Edwards⁴ was unable to differentiate fecal from nonfecal coliform strains.

We found as many varieties of coliform bacteria in the upper respiratory tract as in the intestinal tract, though the proportion of mucoid strains was higher in the upper respiratory tract (table 1). This bears

2. Parr, L. W.: Coliform Bacteria, Bact. Rev. **3**:1-48, 1939.

3. Topley, W. W. C., and Wilson, G. S.: The Principles of Bacteriology and Immunity, ed. 2, Baltimore, William Wood & Company, 1936.

4. Edwards, P. R.: Relationships of the Encapsulated Bacilli with Special Reference to Bact. Aerogenes, J. Bact. **17**:339, 1929.

out Parr's² assertion that the typical intestinal form is *Esch. coli* whereas the coliform bacteria from other parts of the body, such as the bladder and the upper respiratory tract, are usually of the encapsulated type. This type is also found more frequently in the soil than in feces. Although the strains from the respiratory tract varied somewhat in pathogenicity, no one type appeared to exceed in toxicity. The apparently greater toxicity of these strains as compared with the intestinal strains raises the question of the influence of habitat on pathogenicity (table 2). Another factor affecting the disease-producing ability of these organisms

TABLE 2.—*Comparison in Iridocyclitis-Producing Property of Coliform Bacteria from the Upper Respiratory Tract and from the Feces (K. Pneumoniae), 0.5 Cc. of a Twenty-Four Hour Culture Injected Intravenously Into Rabbits Being Used (Berens and Nilson¹)**

Intensity of Iridocyclitis Produced by Strains from Upper Respiratory Tract			Intensity of Iridocyclitis Produced by Strains from Feces		
Rabbit No.	4 Hours	24 Hours	Rabbit No.	4 Hours	24 Hours
1	++	0	12	0	0
2	++	++	13	0	0
3	++	+	14	±(½)	0
4	+	++	15	±(½)	0
5	++	+	16	+	+
6	++	++	17	0	0
7	++	+	18	+	+
8	++	Animal dead	19	+(½)	+
9	++	+, animal dead in 48 hours	20	+	++
10	++	++			
11	+++	++, animal dead in 30 hours			
Average intensity	2.0 plus	1.4 plus		0.5 plus	0.55 plus
Mortality.....		27%			0%

* The designation ± indicates a very slight congestion; +, a definite congestion in the vessels of the iris; ++, marked engorgement of the vessels in the iris; +++, marked congestion of the iris, marked circumcorneal congestion, edema and clouding of the iris with or without small hemorrhages; +++++, the same as +++ with the addition of exudate in the anterior chamber.

may be seasonal, a seasonal variation having been noted during the course of our experiments. Whether such a variation is caused by changes in the organisms or in the resistance of the hosts is an open question. From the clinician's viewpoint, determination of the pathogenicity of an organism supersedes classification in importance. The following means are generally used to classify the coliform bacteria: growth on Levine's eosin-methylene blue agar, Simmons' citrate agar and blood agar; Voges-Proskauer and methyl red tests, and the production of indole.

PATHOGENICITY OF COLIFORM BACTERIA

A. For Animals.—The pathogenicity of certain members of the group for animals is well known, particularly in regard to diseases of the intestinal tract. Parr² quoted Ten Broeck as stating that "it is extremely difficult to evaluate the importance of the colon group in animal pathology but that they take the place of streptococci in man, i. e., they are often secondary invaders that complicate infection." Parr also pointed out that the coliform bacteria involved in diseases of animals are usually



Fig. 1.—Iridocyclitis in the anterior segment of a rabbit eye twenty-four hours after an intravenous injection of 1 cc. of coliform bacteria. The animal lived for twenty-four hours. At the end of six hours the eyes showed marked injection of the vessels of the iris and clouding of the anterior chamber. Pathologic examination revealed edema, congestion of the vessels and areas of hemorrhage in the ciliary processes. Fibrin and a few polymorphonuclear leukocytes were scattered through the interstitial tissues of the iris and the ciliary processes. The epithelium of the ciliary processes was necrotic in a few places. In the anterior and posterior chambers a fine granular precipitate was noted. Gram-negative bacteria were observed in vessels of the ciliary processes in another section from the same animal.

in the mucoid phase and more pathogenic for young than for mature animals. The natural resistance of the animal seems to play an important part in its susceptibility to infection due to coliform bacteria, though some immunity may be acquired through injections of immune serum. Some of the diseases caused by coliform bacteria are mouse typhoid, scours in calves, the infectious diarrhea of chicks, abortion in sheep and mastitis in cows. In experimental infections produced by intravenous, intraperitoneal or subcutaneous injection of the live organisms, coliform bacteria appear to be fairly toxic for laboratory animals. In 1911 Guillery⁵ reported the production of uveitis in rabbits by the intravenous

TABLE 3.—*Reaction of Immunized Rabbits* to Intravenous Injections of Coliform Bacteria Freshly Isolated from the Upper Respiratory Tract*

	Number of Previous Injections	Days Since Last Injection	Amount of Fresh Culture, Cc.		Reaction
Test rabbit 812.....	6	2	1.0	+	Iritis in 3 hours, negative in 24 hours
Control rabbit 818...	0	..	1.0	++	Iritis in 3 hours, + iritis in 24 hours
Test rabbit 563.....	1	21	1.0	+	Iritis in 4 hours, subsiding in 24 hours
Control rabbit 574...	0	..	1.0	++	Iritis in 4 hours, animal dead in 18 hours
Test rabbit 807.....	1	4	0.5	±	Iritis in 3 and 18 hours
Control rabbit 810...	0	..	0.5	+++	Iritis in 3 hours, ++ in 18 hours
Test rabbit 809.....	1	4	0.3	±	Iritis in 3 and 18 hours
Control rabbit 811...	0	..	0.3	++	Iritis in 3 and 18 hours
Test rabbit 873.....	3	3	0.3		No iritis in 4 and 24 hours
Control rabbit 886...	0	..	0.3	++	Iritis in 4 hours, good + iritis in 24 hours
Test rabbit 874.....	4	3	0.3	±	Iritis in 4 hours, negative in 24 hours
Control rabbit 886...	0	..	0.3	++	Iritis in 4 hours, good + iritis in 24 hours
Test rabbits 876, 877, 879 and 880	3	44	0.3		No iritis in 4 and 24 hours
Control rabbits 884 and 885	0	..	0.3	++	Iritis in 4 hours, + iritis in 24 hours

* Rabbits having received one or more small intravenous doses of either culture or filtrate of an iritis-producing upper respiratory tract coliform bacillus.

injection of filtrates of "ferment-producing" organisms. He deduced that the filtrates of certain of these organisms had an affinity for the uveal tract. His work was later confirmed by Woods,⁶ who produced "chronic infiltrative uveitis" with *Bacillus prodigiosus*, an organism somewhat similar to the coliform bacteria in that it is a gram-negative coccobacillus occasionally found in the intestinal tract. Like us, he was able to produce immunity in rabbits by repeated small intravenous doses

5. Guillery: Ueber Fermentwirkungen am Auge und ihre Beziehungen zur sympathischen Ophthalmie, Arch. f. Augenh. 48:242, 1911; Untersuchungen über Uveagifte, ibid. 78:11, 1914.

6. Woods, A. C.: Ocular Anaphylaxis: The Reaction to Perfusion with Specific Antigen, Arch. Ophth. 45:557, 1916.

of bacterial filtrate. From these reports it is evident that some strains of coliform bacteria are pathogenic for animals.

Transitory acute iridocyclitis was produced in rabbits by intravenous injections of cultures with smaller amounts and in a higher proportion of animals when coliform bacteria obtained from the upper respiratory tract were used than when other types of bacteria ordinarily found in this tract were used^{1b} (fig. 1).

Bacteria-free filtrates also produced iridocyclitis, and the results obtained from intravenous injections of these filtrates and of the original cultures were identical. Of particular interest was the marked difference in pathogenicity between coliform bacteria from the upper respiratory tract and fecal strains, the former being more lethal as well as possessing a greater iritis-producing ability. The fact that partial or complete immunity could be produced in rabbits by small intravenous doses of either cultures of live coliform bacteria or their sterile filtrates suggested the possibility of using autogenous vaccines for patients harboring these organisms (table 3).

B. For Man.—The pathogenicity of coliform bacteria for man is more difficult to determine. In the case of definite lesions or an acute disease the diagnosis is comparatively simple. Baehr, Schwartzman and Greenspan⁷ summarized the knowledge of the Friedländer bacillus as the etiologic agent in a number of diseases. Belk⁸ reported 18 cases of pulmonary infection (lobar pneumonia and pulmonary abscesses) caused by the Friedländer bacillus, in all of which the patient died. Thygeson⁹ recently reported on 94 cases of conjunctivitis and keratitis, in 11 of which he attributed the disease to some member of the coliform group. Parr² referred to reports on *Proteus morgani* as the etiologic agent in diarrhea in infants, dysentery in adults, infections of the intestinal and of the urinary tract, meningitis, infections of wounds and septicemia. The Friedländer bacillus has been found in association with similar diseases but more predominantly in the upper respiratory tract. Other members of the coliform group have also been reported as causing the diseases mentioned, in addition to which they have been held responsible for food poisoning in certain cases, infectious arthritis and "rare cases of infectious dermatitis." In connection with the reports of food poisoning caused by some member of this group, Parr said: "If coliform organisms can produce a toxin, as seems amply demonstrated, it is a little odd that more intoxications with this toxin have not occurred; it may well be

7. Baehr, G.; Schwartzman, G., and Greenspan, E. B.: *Bacillus Friedländer Infections*, Ann. Int. Med. **10**:1788 (June) 1937.

8. Belk, W. P.: *Pulmonary Infections by Friedländer Bacillus*, J. Infect. Dis. **38**:115-126, 1926.

9. Thygeson, P.: *The Cultivation of Conjunctivitis—and Keratitis-Producing Agents on the Chorioallantoic Membrane of Chick Embryo*, Am. J. Ophth. **23**: 1217, 1940.

that the human adult is relatively resistant to it." While this is probably so, one should not lose sight of the fact that there has been a tendency to overlook the probable pathologic significance of this group of organisms in chronic diseases, even as secondary invaders. One of its most toxic members, the Friedländer bacillus, has been generally regarded as a normal habitant of the upper respiratory tract and of little importance.³

The following opinions on the coliform bacteria in infections of the upper respiratory tract were obtained by personal communication with physicians in various parts of the country.

1. J. R. Lindsay :

I have not paid particular attention to coliform bacteria in connection with infections of the upper respiratory tract and therefore can give no definite information. I have, however, obtained pure cultures of the Friedländer bacillus in rare cases of empyema of the maxillary sinus. The condition has responded quickly to irrigation. Organisms of the coliform group are sometimes observed in my routine cultures of material from the throat and from the paranasal sinuses in cases of chronic suppuration; that is, *Bacillus proteus* and *Esch. coli* have been reported. I have thought that they were not the primary cause of the suppuration but were secondary invaders, appearing after drainage had been impeded. In the case of the Friedländer bacillus, however, it appeared that the infections were subacute and it seemed probable that this organism originated the empyema.

2. S. J. Crowe :

I have observed many cases of infection of the accessory nasal sinuses in which some organism of the coliform group was obtained on culture, but I have always thought that these organisms were secondary invaders and were not responsible for lesions of the eyes, joints or kidneys.

3. G. M. Coates :

I can say only that I have no notes of cases of infection of the upper respiratory tract associated with organisms of the coliform group. Occasionally I obtain a culture positive for the Friedländer bacillus, *Esch. coli* or *B. proteus*, and I have usually considered the last-named organism a causative agent. None of the cases that I can think of were of ocular lesions.

4. A. W. Proetz :

To the best of my recollection I have observed no cases of infection in the upper respiratory tract attributable to coliform bacteria. This does not mean, however, that such infections have not existed, for unless an infection of the upper respiratory tract has some unusual feature no cultures are made in my office. Certainly none of the more unusual or intractable infections which have come to my notice have been of this character.

5. R. Kramer :

I have had some rather interesting experiences with *Esch. coli* in infections of the sinuses, particularly in relation to associated ocular conditions. In a few cases a pure culture of *Esch. coli* was obtained from material from the sinuses and there was a striking cure of the ocular disease when the sinus infection was

eradicated. I have the impression, unsubstantiated by statistics, that *Esch. coli* causes a focal infection oftener than the frequency of its presence in cases of uncomplicated infection would lead one to expect. It would be interesting to check this by actual count.

6. H. T. Hyman:

Dr. J. Felsen isolated *Bacillus mucosus capsulatus* (*K. pneumoniae*) and non-hemolytic streptococci from the sinus exudate of a patient with recurrent parenchymatous keratitis. The former organism is, according to my experience, particularly apt to cause focal difficulties.

ATTEMPTS TO ESTABLISH AN ETIOLOGIC RELATION IN INDIVIDUAL CASES

Because of the difficulty of determining the presence or the severity in chronic disease, which may be latent or hidden, the use of so-called normal controls has proved unsatisfactory. Therefore, it has been necessary to seek proof of an etiologic relationship of infection by indirect methods, some of which are discussed hereafter.

Cutaneous Tests.—The value of cutaneous tests as an aid to the determination of pathogenicity appears doubtful. Chapman and Berens¹⁰ noted that in general there was little agreement between the toxicity of an organism (as determined by in vitro tests, which showed a fairly close correlation with animal inoculation) and its intradermal effect. With the coliform group the correlation was even less than with other types of bacteria. Short, Dienes and Bauer¹¹ maintained that "variations in skin reactions may be explained by differing irritability of the patient's skins, natural toxicity of the bacterial species, or possibly by a sensitization to certain bacterial groups." Chapman and Berens¹⁰ pointed out that there is no great difference in the proportion of positive cutaneous reactions between patients with ocular diseases and control groups, which confirms the findings of Steinberg and Wiltsie,¹² who obtained cutaneous reactions with toxic filtrates of *Esch. coli* in all of 60 normal children and 40 normal adults, although 4 of 11 patients with pyelitis in whom *Esch. coli* was the infecting organism did not react to the filtrate. Solis-Cohen,¹³ in comparing the value of the cutaneous tests

10. Chapman, G. H., and Berens, C.: Comparison of Intradermal Tests with Agglutinability and Certain in Vitro Tests of Streptococci, *Micrococcus Catarhalis*, and Colon Bacilli Isolated from Persons Suspected of Having Chronic Infection, *J. Lab. & Clin. Med.* **24**:601, 1939.

11. Short, C. L.; Dienes, L., and Bauer, W.: Autogenous Vaccines in Rheumatoid Arthritis: A Clinical Study and Critique, *Am. J. M. Sc.* **187**:615, 1934.

12. Steinberg, B., and Wiltsie, C. O.: Skin Reactions to the Colon Bacillus and Its Toxic Products, *J. Immunol.* **22**:109, 1932.

13. Solis-Cohen, M.: Comparison of the Relative Values of Intracutaneous Skin Test and of Pathogen-Selective Culture in Selecting Bacteria for Vaccines from Mixed Infections, *Am. J. Clin. Path.* **3**:305, 1933.

with that of his pathogen-selective method, concluded that "there is probably no relationship between hypersensitiveness in the host to the exogenous and endogenous toxins of a given organism and the pathogenicity of such organism for the host." Recently Branham, Hitchens and Root¹⁴ reported on a series of experiments in which they studied the significance of positive cutaneous reactions to meningococcus toxins in a group of 490 boys among whom there had been an outbreak of meningococcal meningitis. The blood from 50 of these boys was tested for bactericidal and phagocytic effects on meningococci. There was no significant correlation between the results of the tests and the reactions to intracutaneous injections of meningococcus toxin. Of interest, however, was the suggestion of seasonal influence on reactivity, the reactions being less pronounced in the early summer. Although cutaneous reactions seem on the whole to be in no way related to the presence of infection, there may be some basis for using them as a measure of acquired immunity to coliform bacteria, since the reaction tends to diminish with vaccine therapy.¹⁵

Agglutination Tests.—Agglutination tests as indicators of pathogenicity are also of questionable significance. Recently Falk and Smith,¹⁶ working with therapeutic antimeningococcus preparations with mice, observed that certain preparations showing no agglutinins were on repeated testing able to protect mice as well as preparations showing marked agglutination. Eastwood¹⁷ pointed out that active immunity could be acquired without the production of serologic antibodies, while Teale¹⁸ showed that an immunized animal could clear various organisms from the blood in the absence of agglutinins, bactericidins and antibodies protective against the invading micro-organisms. Gilbert and Dacey¹⁹ reported the recovery of *Brucella abortus* from the blood clot of a

14. Branham, S. E.; Hitchens, A. P., and Root, M. B.: A Study of the "Skin Test" with Meningococcal Toxins in a Group of Boys, *J. Bact.* **41**:55, 1941.

15. Mateer, J. G.; Baltz, J. I.; Fitzgerald, J., and Woodburne, H. L.: Colon Bacillus Vaccine Therapy as Related to Chronic Functional Diarrhea, Chronic Headache, Chronic "Toxic Vertigo" and "Unstable" Colon (Non-Ulcerative Colitis), *Am. J. Digest. Dis. & Nutrition* **2**:621, 1935.

16. Falk, C. R., and Smith, S. L.: The Relationship of Mouse-Protective Activity to the Agglutinin and Precipitin Content of Therapeutic Antimeningococcal Preparations, *J. Bact.* **41**:56, 1941.

17. Eastwood, A.: The Nature of Antibodies, *J. Hyg.* **33**:259, 1933.

18. Teale, F. H.: Some Observations on the Relative Importance of the Reticulo-Endothelial Tissues and the Circulatory Antibody in Immunity: I. Bacterial Immunity in Relation to the Role Played by the Circulating Antibody and the Tissues Following Intravenous Introduction of the Bacteria, *J. Immunol.* **28**:133, 1935.

19. Gilbert, R., and Dacey, H. G.: The Isolation of an Organism of the Abortus-Melitensis Group from a Blood Clot, the Serum of Which Failed to Give Agglutination with *B. Abortus*, *J. Lab. & Clin. Med.* **17**:345, 1932.

patient whose serum did not agglutinate this organism. Autoagglutination makes it impossible to use agglutination tests in certain instances. Stiles and Chapman²⁰ showed that in general agglutinable cultures did not give stronger in vitro toxic reactions than did inagglutinable cultures. They found that certain cultures which were highly toxic according to in vitro tests were entirely inagglutinable. On the other hand, they noted that certain serums agglutinated a wide variety of bacteria, some in high dilution, suggesting that "agglutination was as much a function of the serum as of the bacteria." Rawls and Chapman²¹ found that streptococci which were toxic according to in vitro tests but inagglutinable by the patient's serum had greater power to produce arthritis in rabbits than did toxic strains which were agglutinable by the patient's serum.

Determination of the electrophoretic mobility of coliform strains has been found more applicable to group testing than to the testing of individual strains. Using this method, Stiles and Chapman²⁰ tested 2,148 strains of coliform bacteria and found agreement with agglutinability in 67.4 per cent of the cultures. They also found that there was an agreement of less than 40 per cent between cutaneous tests and agglutination tests in the coliform group. Hence, it would seem that the ability of a patient's serum to agglutinate an autogenous coliform strain would give little indication as to its etiologic significance.

*Solis-Cohen Pathogen-Selective Method.*¹³—This method proposed for selecting pathogens is based on the power of toxic bacteria to survive the bactericidal power of the patient's blood. Although the method appears to be sound theoretically, it has not been shown to be reliable.²²

Complement Fixation Method.—A general positive correlation between the complement-fixing properties of unheated blood serum and the electrophoretic mobility of the colon bacilli isolated from the feces of the person from whom the blood was obtained has been shown by Chapman²³ and his associates. However, in using a wide variety of bacterial antigens they found that the complement fixation reactions were not highly specific. Cross fixation, difficulty in titrating and preserving antigens, variability in anticomplementary properties of different

20. Stiles, M. H., and Chapman, G. H.: Relationship Between Agglutinability and Certain in Vitro Tests of Staphylococci, Streptococci and Colon Bacilli Isolated from Persons Suspected of Having Chronic Infection, *J. Lab. & Clin. Med.* **24**:620, 1939.

21. Rawls, W. B., and Chapman, G. H.: Experimental Arthritis in Rabbits, *J. Lab. & Clin. Med.* **27**:49, 1935.

22. Stuart, C. A., and others: Antigenic Relationships of Coliform Bacteria, *J. Bact.* **40**:101, 1940. Short, Dienes and Bauer.¹¹

23. Chapman, G. H.; Berens, C.; Lieb, C. W.; Rawls, W. B., and Stiles, M. H.: Examination of Cultures from Persons Suspected of Having Chronic Infection, *Am. J. Clin. Path.* **9**:491, 1939.

blood specimens and lack of complement-fixing power in certain diseases prevented the successful application of this method.

Comment.—From the foregoing discussion it would appear that at present there is no satisfactory method for determining the pathogenicity of a coliform strain recovered from a patient with chronic disease. Therefore, it seems necessary to follow the unsatisfactory procedure of determining the presence of coliform bacteria in a focus not ordinarily considered to be their habitat, to attempt to eliminate these bacteria by immunization, chemotherapy or other means and to make careful bacteriologic examinations in conjunction with clinical studies.

CLINICAL OBSERVATION

Cultures taken from the upper respiratory tract of 411 patients with ocular diseases or complaints showed the presence of some member of the coliform group of bacteria in 102 (24.8 per cent). The material was obtained from one or more of the following sources: nasopharynx, nasal membranes, sinuses, gums, teeth and tonsils. The most common sites were the nasal membranes and the nasopharynx. Until the last three years we rarely prepared autogenous vaccines from these coliform strains from the upper respiratory tract, since the prevalent opinion was that they were of little if any significance as factors in chronic disease. When later, judging from our experimental work and the clinical symptoms of patients harboring these organisms, it appeared that they might be of importance, vaccine therapy was attempted. Although we administered unusually weak dilutions,²⁴ they were of sufficient toxicity to produce severe reactions in many instances. Still weaker dilutions were then prepared, and the results were apparently favorable. Occasionally we encountered a patient who could not tolerate even the minute doses used. Some patients receiving vaccine therapy had cultures at intervals varying from several weeks to six months. Usually these continued to show the presence of coliform bacteria for at least the first six months of treatment. Frequently there was a change in the type found; e. g., a mucoid strain gave place to a nonmucoid variant. In several patients we studied the toxicity of the coliform strain harbored by them over a period of one to two years. We did this by injecting into rabbits a specified amount of the coliform strain isolated from each culture. There seemed to be a tendency for the strains to diminish in toxicity as treatment progressed and larger amounts of vaccine could be tolerated. In a number of instances the coliform bacteria disappeared entirely and the patient remained constantly free of the organism, as demonstrated by repeated cultures (table 4). In

24. From a suspension of 1 billion organisms per cubic centimeter, thirty-eight consecutive dilutions were prepared.

TABLE 4.—*Progress Noted During Vaccine Therapy of Infections of the Upper Respiratory Tract Due to Coliform Bacteria*

Miss G. A. Migraine, Endophthalmitis Both Eyes, Chorioretinitis Left Eye	Mrs. McL. Grade III Angiosclerosis of Retinal Arteries with Hemorrhages, Chronic Ethmoiditis on Left	Mr. J. H. Incipient Cataract Right Eye, Hypothyroidism, Chronic Sinusitis, Asthenopia
1/25/40: <i>A. aerogenes</i> in nasopharynx; $\div\div$ iritis in rabbits; rabbits very ill and died in 24 hours	11/17/35: <i>A. aerogenes</i> in nose; $\div\div$ iritis in rabbits	9/26/39: <i>A. aerogenes</i> in nasopharynx
3/20/40: <i>A. aerogenes</i> in nasopharynx; $\div\div$ iritis in rabbits	9/ 4/40: Nonlactose fermenter in nasal membranes; mild — iritis in rabbit	8/ 6/40: <i>Esch. coli</i> in nasopharynx
5/25/40: <i>A. aerogenes</i> in nasopharynx; $\div\div$ iritis in rabbits	2/13/41: No coliform bacteria in nose or nasopharynx	12/ 9/40: No coliform bacteria in nose or nasopharynx
9/21/40: <i>A. aerogenes</i> in nasopharynx; \pm iritis in rabbits	Result: Some gradual improvement in condition of sinuses and nasal membranes and in general health coincident with disappearance of coliform bacteria, but more rapid improvement from operation on septum	Result: Systemic improvement, decrease in postnasal drip, improvement of asthenopia
3/19/41: No coliform bacteria in nose or nasopharynx		
4/23/41: No coliform bacteria in nose or nasopharynx		
Result: Systemic and ocular improvement coincident with disappearance of coliform bacteria		
Mrs. M. B. Hay Fever, Recurrent Epileptics, Central Chorioretinitis, Bilateral Ethmoiditis	Mrs. S. K. Glaucoma (Chronic Secondary), Chronic Uveitis, Cataract	Miss B. W. Chronic Uveitis Right Eye, Beginning Complicated Cataract Right Eye
6/ 2/37: <i>A. aerogenes</i> in right nostril; \div iritis in rabbit	10/ 5/39: <i>Esch. coli</i> in nose	9/13/39: <i>B. proteus</i> in nose
11/27/38: No coliform bacteria in nose or nasopharynx	1/ 9/41: No coliform bacteria in nose or throat	9/18/40: <i>A. aerogenes</i> in nasopharynx; marked $\div\div$ iritis in rabbits
3/16/40: <i>B. pyocyaneus</i> in right eye	Result: Uveitis improved and tension more easily controlled	4/16/41: <i>B. proteus</i> in nose
1/ 7/41: No coliform bacteria in nose or nasopharynx		Result: Attacks of uveitis less frequent and milder
Result: Eyes much improved		
Miss C. C. (Case 1) Uveitis Right Eye, Chronic Ethmoiditis on Right, Secondary Glaucoma Right Eye	Mr. S. P. Chronic Endophthalmitis Both Eyes, Chronic Hyperplastic Ethmoiditis, Retrobulbar Neuritis, Depression	Mr. F. B. G. Endophthalmitis, Recurrent Conjunctivitis
10/22/36: Cornell Research Laboratory— <i>A. aerogenes</i> in nasopharynx; no vaccine prepared	12/ 2/38: <i>Esch. coli</i> in sputum and nasopharynx	6/30/36: <i>A. aerogenes</i> in nasopharynx; $\div\div\div$ iritis in rabbits; very toxic for rabbits
10/20/36: Clinical Research Laboratory— <i>A. aerogenes</i> in nose; marked iritis in rabbits; vaccine prepared	4/12/39: <i>Esch. coli</i> in nasopharynx	8/ 7/36: <i>A. aerogenes</i> in nasopharynx; $\div\div\div$ iritis in rabbits
5/10/37: Use of <i>A. aerogenes</i> vaccine started	11/ 7/39: <i>Esch. coli</i> in nasopharynx	1/ 9/37: <i>A. aerogenes</i> in nasopharynx; $\div\div$ iritis in rabbits; not as toxic as formerly
9/25/39: <i>B. proteus</i> in nose and throat (office laboratory); new vaccine prepared	6/14/40: <i>Esch. coli</i> in nasopharynx; smaller number than usual; growth not as luxuriant	1/ 7/39: <i>A. aerogenes</i> in nasopharynx; — iritis in rabbits; new vaccine prepared
Result: Uveitis cured; ethmoiditis improved	4/23/41: No coliform bacteria in nose or nasopharynx	8/12/39: <i>Esch. coli</i> in nasopharynx; \div iritis in rabbits
	Result: Marked improvement in ocular and in general condition	1/10/40: No coliform bacteria in nose or throat
		3/ 7/40: No coliform bacteria
		6/14/40: No coliform bacteria
		Result: General improvement

contrast, several patients to whom we were unable to administer a coliform bacteria vaccine because of severe reactions or other contraindications retained the organism over a period of years.

The diagnoses for the 102 patients harboring some coliform bacteria in the upper respiratory tract revealed the following facts: Intraocular infections comprised 68 per cent of the 102 diagnoses (table 5). Included in the group were some patients who also had cataract (10.8 per cent). Only 3 per cent of the patients had cataract without intraocular signs of chronic inflammation. Extraocular disease was present

TABLE 5.—*Ocular Conditions Found in 102 Patients Harboring Upper Respiratory Tract Coliform Bacteria*

Ocular Condition	Number of Patients	Percentage
Intraocular disease *.....	58	57.2
Uveitis.....		68
Iritis.....		
Iridocyclitis.....		
Endophthalmitis.....		
Choroiditis.....		
Chorioretinitis.....		
Hemorrhagic retinitis.....		
Intraocular disease and cataract.....	11	10.8
Cataracts only.....	3	3.0
Extraocular disease.....	23	22.5
Chalazion.....		13.8
Hordeolum.....		
Keratitis.....		
Meibomianitis.....		
Conjunctivitis.....		
Episcleritis.....		
Blepharitis.....		
Marginal ulcerative keratitis.....		
Ill defined disease or symptoms.....	7	6.5
Retrobulbar pain.....		6.5
Asthenopia, etc.....		
Total.....	102	100.0

* Many of the patients had some extraocular disease.

in 22.5 per cent of the patients, and 6.5 per cent of the diagnoses were indefinite, the patient's symptoms apparently being unassociated with any specific disease of the eye (e. g. migraine). This high incidence of intraocular diseases is of interest, since many of these diseases are suspected of being infectious in origin, although up to the present coliform bacteria apparently have been ignored as one of the possible etiologic factors.

In an early, considerably smaller series it appeared that the number of cases of cataract associated with coliform bacteria infection of the upper respiratory tract might prove significant. The present series, however, showed no significant difference. Cataract was present in 13.7 per cent of 102 patients harboring upper respiratory tract coliform

bacteria, as compared with 18.1 per cent of 309 patients showing no such bacteria.

Vaccine Therapy.—The results of vaccine therapy are obviously difficult to evaluate. The fact that some of the patients submitted to operation on the upper respiratory tract, that other forms of treatment were often included and that most diseases tend to improve spontaneously all add to the difficulty.

The following case histories are submitted as examples of the results of coliform bacteria vaccine therapy as observed by us.

CASE 1.—Miss C. C., aged 35, was first examined in September 1936. At that time she had retrobulbar neuritis of the right eye in addition to chronic uveitis of four months' duration. This had begun with iritis, which had been treated. A Wassermann test of the blood, a blood count, urinalysis, a test of the basal metabolism and roentgen examination of the sinuses and of the teeth showed no abnormality. A roentgenogram of the chest showed "spots of calcium density in the

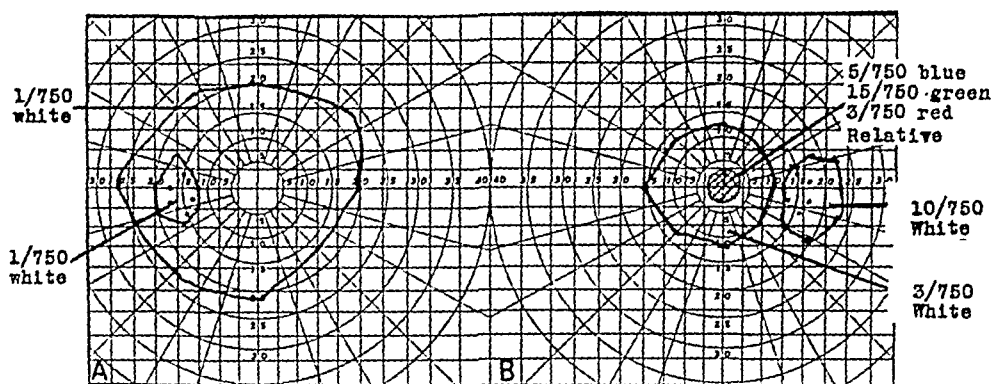


Fig. 2.—The visual fields of Miss C. C. (case 1), aged 35, on Sept. 21, 1936 (A, left eye; B, right eye). There was retrobulbar neuritis of the right eye, with chronic uveitis.

left first and second interspaces anteriorly, suggesting old minimal tuberculous lesions. There was evidence of a little bilateral apical pleural thickening." However, an intradermal tuberculin test gave negative results. The vision of the right eye was 20/200 + 1 with pinhole vision of 20/70, and of the left eye, 20/20 with pinhole vision of 20/15. The tension of the right eye was 16 mm. and of the left eye 19 mm. when measured with a Schiötz tonometer. The central and peripheral fields of the right eye were markedly contracted (fig. 2).

The medical history to the time of the first attack of iritis revealed nothing important except an operation in 1921, when the right middle turbinate was partially removed and a partial ethmoidectomy and a complete tonsillectomy were performed.

At the time the patient was first seen by us, Dr. James Evans suggested that the physiology of the nose could be improved by infracture outward of both middle turbinates and removal of a small portion of the left middle turbinate. This operation was performed, following an iridectomy and aspiration of the anterior chamber of the right eye. The aqueous was cultured and found to be sterile.

Material for culture was taken from the upper respiratory tract and studied at two laboratories (Clinical Research Laboratory and Department of Pathology,

Cornell University Medical College). Both reported the presence of *A. aerogenes*, one strain of which was injected intravenously into rabbits, producing severe acute iridocyclitis. Toxic strains of *Streptococcus viridans* were also recovered from the nasopharynx. Separate vaccines were prepared from the aerobacter strain and from the streptococcus strains, and that from the latter was at first used for treatment.

The patient had received nonspecific protein therapy before seeing us, and this was continued for a short time. In addition, an alkaline diet was instituted, thyroid in small doses and vitamin B complex were given and staphylolysin in physiologic solution of sodium chloride was given intranasally. She was found to be allergic to hyoscine, duboisine and atropine. In spite of treatment, which included vaccine therapy, iridectomy and a nasal operation, she continued to have frequent severe attacks of iritis although there was improvement in her health. In May 1937 use of the streptococcus vaccine was discontinued and a test dose of the *A. aerogenes* vaccine given (0.05 cc. of decimal dilution 42). This was followed by severe acute iridocyclitis associated with a great deal of pain and intense nausea. Two months later a much weaker dose (0.01 cc.) of the same vaccine was given; doses were then given at weekly intervals, being increased slowly. Although by December 1937 there was a marked improvement in the uveitis, the attacks being less frequent and less painful, the vision had decreased to 1/200 in the right eye and was 20/15 in the left eye. From December 1937 until September 1939 there were only a few mild recurrences of iritis, which appeared to be associated with colds or nasal treatments. The exudate on the anterior part of the lens capsule had largely disappeared. When the patient was seen in 1939 there were no cells in the aqueous, the aqueous beam was invisible and the eye seemed free from inflammation. The vision had improved in the right eye to 20/100 with correction and was 20/15 — 1 in the left eye. Cultures of material taken from the nose and throat showed a growth of *B. proteus*. A vaccine of this organism was substituted for the *A. aerogenes* vaccine.

On May 19, 1941 the vision was 20/100 in the right eye and 20/15 in the left eye. Biomicroscopic examination revealed no signs of inflammation in either eye.

Comment.—The uveitis in the right eye seemed to be unaffected by nonspecific protein therapy, nasal operation or use of a streptococcus vaccine. A small dose of *A. aerogenes* vaccine apparently caused a severe attack of uveitis. Improvement in the ocular inflammation coincided with the administration of smaller doses of *A. aerogenes* vaccine. There had been no attacks in two years until last winter, when the patient had a mild attack of iridocyclitis associated with influenza.

CASE 2.—Mr. H. B., aged 44, was first examined on April 21, 1938, at the suggestion of Dr. Harold T. Hyman. His chief complaint was failing vision. In the right eye this was accompanied with pain; in the left eye it was first noticed in 1928. The medical history included some sinus infection and migrainous headaches. He had received tuberculin therapy and foreign protein therapy for parenchymatous keratitis of the left eye, which developed in 1928 and finally resulted in loss of reading vision. A trephination with peripheral iridectomy had been performed on the left eye.

A general physical examination gave negative results except to reveal a basal metabolic rate of minus 18, a positive intradermal reaction to tuberculin and a

chronic inflammation of the membrane in the right nostril; mucopus was obtained from the left antrum and there was a history of a diagnosis of chronic sinusitis in 1930.

Vision in the right eye was 20/20 — 2 and in the left eye 2/200. There was a dense opacity in the stroma of the right cornea in the upper temporal quadrant and in the pupillary area (fig. 3). In the left eye there was a diffuse opacity in the stroma of the cornea which obscured the view of the iris. On April 27, 1938 the visual fields of the left eye showed a central scotoma and in the right eye a depressed area for a 1 mm. test object was observed in the upper temporal quadrant.

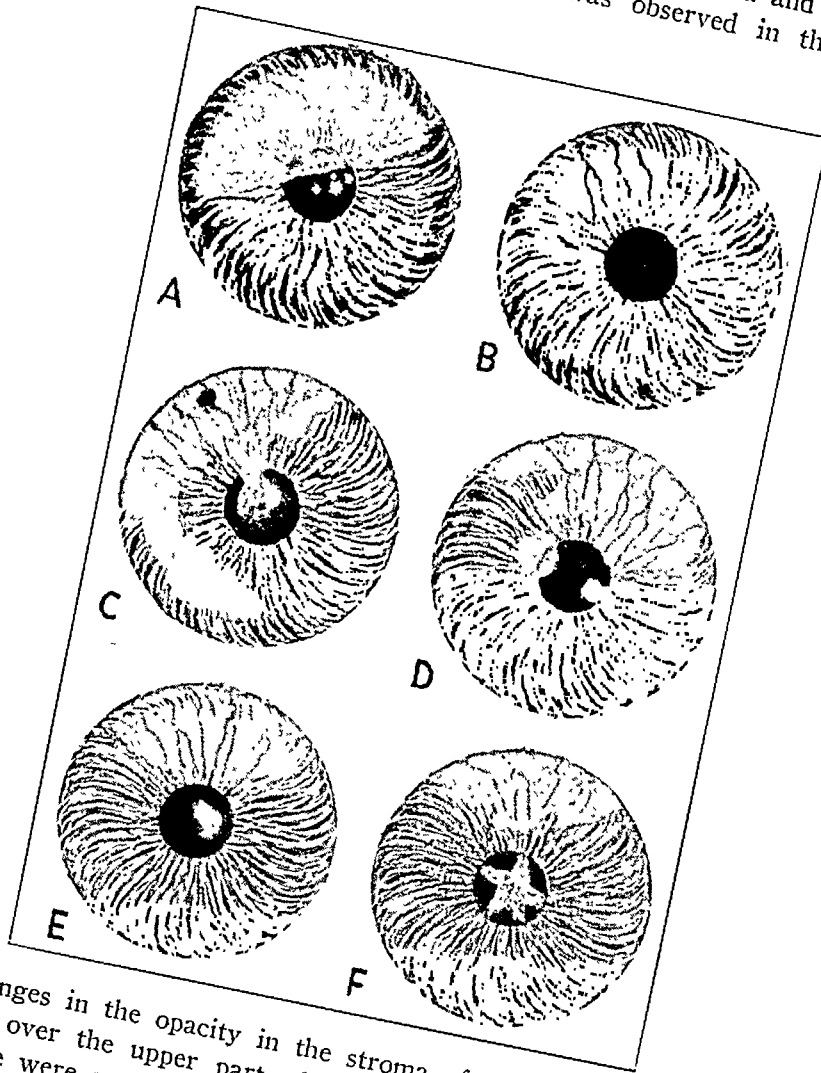


Fig. 3.—Changes in the opacity in the stroma of the right cornea in case 2. *A*, diffuse haze over the upper part of the right cornea, extending from 2 to 8 o'clock. There were centrally located irregularly rounded grayish opacities in the corneal stroma. *B*, central infiltrations were absent (Sept. 9, 1938). There was one area in the upper temporal quadrant with blood vessels extending deep into it. A deep type of sclerosing keratitis was present. Vision was 20/15, and the near point of accommodation was 180/300. *C*, there was one small hemorrhage. The vessels visible before were not seen, but there was dense infiltration in the pupillary area. *D*, on Oct. 17, 1939 vision was 20/15. *E*, on November 6, 1941 vision with correction was 20/40, with pinhole vision of 20/30. *F*, on May 23, 1941 vision with correction was 130/500.

In 1938 Dr. H. T. Hyman and Dr. R. Kramer believed the sinuses normal. On Feb. 20, 1939 chronic hyperplasia of the membrane in the left antrum was diagnosed. A culture of exudate from the maxillary sinus by Dr. Kramer revealed *Staphylococcus aureus* and *Esch. coli*. A vaccine was prepared and administered by Dr. Hyman.

On April 10 a bilateral ethmoidectomy and sphenoidectomy and a Caldwell-Luc operation on the left antrum were performed by Dr. Kramer. Colon bacilli and staphylococci were observed in a culture of material taken at the time of operation.

On June 8 cultures of specimens from the nasal membranes on the right side showed *Esch. coli* and toxic *Staph. aureus*. When injected intravenously into rabbits the *Esch. coli* strain produced a 2 plus iritis which persisted for forty-eight hours. Toxic staphylococci but no streptococci toxic according to in vitro tests were found in a culture of nasopharyngeal secretion taken on the same day.

On June 12 a culture of exudate from the right ethmoid sinus showed a non-lactose fermenter (probably a degenerate strain of *Esch. coli*). When injected

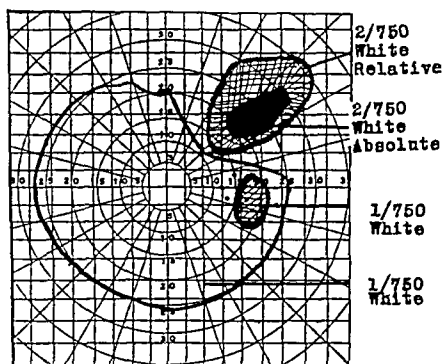


Fig. 4.—The visual field of the right eye of Mr. H. B. (case 2), aged 44, on Nov. 8, 1940. The diagnosis was parenchymatous keratitis and retrobulbar involvement of the optic nerve.

into rabbits this strain produced only a mild iritis which had appeared in six hours and had subsided entirely in twenty-four hours.

On Jan. 17, 1940 Dr. Hyman said: "I think the improvement in Mr. B.'s eyes phenomenal. He is still being given the colon bacillus vaccine."

On May 17 the patient accepted a correction for the right eye of -0.25 D. sph. $+1.00$ D. cyl., axis 120; vision was 20/20.

On June 20 Dr. Hyman said, "I think that we can now unreservedly express ourselves as having collaborated in the production of a sort of minor miracle."

On October 29 a cold developed which lasted for seven weeks, during which time the vision was only slightly affected, mainly by mild retrobulbar neuritis. A culture by Dr. Kramer of material from the right antrum showed nonhemolytic streptococci and *Staph. aureus* (fig. 4).

On Feb. 10, 1941 a culture of secretion from the right nostril showed mucoid coliform bacteria (*K. pneumoniae*), which produced a marked 3 plus iritis in rabbits in four hours that was severe 2 plus iritis in twenty-four hours. The patient had a marked central corneal opacity in the right eye after a severe flare-up of his chronic sinusitis.

On March 26 Dr. Hyman said: "Dr. J. Felsen reported *B. mucosus capsulatus* (*K. pneumoniae*) and a nonhemolytic streptococcus in a culture of material from the sinus. A new vaccine was prepared."

On April 8 a culture from the conjunctival membrane showed coliform bacteria of intermediate type. A 1 per cent ointment of sulfadiazine (2-[paraaminobenzenesulfonamido]-pyrimidine) was prescribed for the eyelids.

On May 6 cultures of ocular and nasal secretion showed a pure growth of coliform bacteria of the same type as those found on April 8.

Comment.—Although H. B. is not free from parenchymatous keratitis he did show an improvement while undergoing vaccine therapy for the infection due to coliform bacteria, in that the corneal opacities in the substantia propria in the pupillary area completely disappeared on four occasions. Two ophthalmologists had said that the opacities in the pupillary area were permanent, and we had feared that they were, as we had never seen such dense opacities disappear completely and the history of the left eye was discouraging.

General treatment included the use of grenz rays, tuberculin therapy, vitamin therapy, chemotherapy and foreign protein therapy. General treatment by Dr. Hyman, which included the administration of 3 Gm. of sulfathiazole (2-[paraaminobenzenesulfonamido]-thiazole) every four hours the first day and 1 Gm. every four hours for four days thereafter, seemed to be less effective than nasal treatment and operation combined with vaccine therapy. What stands out most prominently is the persistence of the coliform bacteria in the sinuses and the possibility that they may be a cause of the keratitis. It should be noted that in the last attack, which was the worst, we obtained a strain of coliform bacteria that was more toxic for rabbits than any of the strains previously tested. We have discovered that the lake in which the patient swims is heavily infected with *Esch. coli*.

CASE 3.—Mr. S. L. P., aged 46, was first examined on Dec. 5, 1930. Diagnoses of chronic endophthalmitis and retrobulbar neuritis were made. On December 9, 1938 a diagnosis of chronic hyperplastic ethmoiditis was made by Dr. S. L. Craig.

The chief complaints were twitching of the left lower eyelid, failing of distant vision, burning of the eyes, lacrimation and the floating of spots across the page during reading. The patient felt that there was a film over his eyes that could be pushed away.

The medical history included removal of the tonsils, constipation, almost constant headaches, devitalization of several teeth, chronic catarrh (postnasal drip) and recurrent attacks of depression.

The vision with correction for compound myopic astigmatism fluctuated between 20/15 and 20/30.

The tension was 17 mm. in both eyes as measured with a Schiötz tonometer, and at no time was it higher than normal.

The central fields exhibited temporary recurrent relative central scotomas for green and blue when the sinuses were most troublesome.

On April 16, 1931 the general physical findings included low grade hyperplastic ethmoiditis and sphenoiditis (Dr. R. T. Atkins). Dr. G. S. Dixon reported: "The ethmoid sinuses are broad and cloudy, especially the left. The region of the sphenoid sinus is highly developed and irregularly cloudy."

A culture of nasopharyngeal secretion revealed *Str. viridans*, *Streptococcus communis*, *Micrococcus tetragenus* and diphtheroid bacilli. From these organisms a vaccine (2 billion per cubic centimeter) was made and sprayed intranasally. Treatment at this time included use of ethylmorphine hydrochloride, use of infra-red light, colonic irrigations, extraction of a tooth, application of phenolized oil to the nasal membranes, use of hot compresses and additional local nasal treatment.

In December 1938 the patient had severe attacks of melancholia and the vision was badly blurred (mild retrobulbar neuritis). He was exceedingly tense and coughed a great deal.

A culture of material from the nasopharynx showed many colon bacilli and nontoxic streptococci. A culture of the sputum revealed many colon bacilli and toxic streptococci. A culture of feces showed a greatly decreased number of colon bacilli (200)²⁵ and a moderate number of fairly toxic streptococci (*Str. viridans*).

A vaccine was prepared from the colon bacilli from the upper respiratory tract. The first dose consisted of 0.03 cc. of no. 42 dilution, and its administration was followed almost immediately by a marked beneficial ocular and general response. The patient continued the vaccine therapy and continued to improve.

Chemical examination of the blood at that time showed a somewhat high content of uric acid and of chlorides. The white cell count was high at all times, ranging from 9,990 to 13,400. Otherwise the blood was normal. The urine showed occult blood with a great deal of mucus. The sedimentation rate and the basal metabolism rate were normal.

On April 12, 1939 a culture of secretion from the nasopharynx showed toxic staphylococci (*Staphylococcus albus*), nonpathogenic streptococci and many colon bacilli. On April 20 staphylococcus toxoid was administered. On May 5 the condition of the nose had improved. On November 7 a culture of nasal secretion revealed toxic staphylococci (*Staph. albus*) and a culture of material from the throat, many colon bacilli and toxic streptococci. A culture of the feces revealed an abnormally low count of colon bacilli. On November 30 treatment with streptococcus and staphylococcus vaccine was started, this vaccine being administered alternately with the colon bacillus vaccine.

On Feb. 13, 1940 the patient was having a severe reaction to each injection of the streptococcus and staphylococcus vaccine and therefore was told to discontinue using it but to continue using the colon bacillus vaccine.

On June 14 a culture of material from the nasopharynx showed toxic streptococci and a few colon bacilli, which grew less abundantly than previously.

On April 23, 1941 colon bacilli could no longer be cultivated and use of the vaccine was discontinued because the patient's eyes and general condition were greatly improved.

Comment.—A patient with endophthalmitis, retrobulbar neuritis, chronic ethmoiditis and recurring attacks of depression was treated with staphylococcus and streptococcus vaccine, colon bacillus vaccine, remedies applied locally to the sinuses, infra-red light, hot baths and massage, bile salts, acidophilus milk, saline solution in subconjunctival injection.

25. Normal is from 50,000 to 100,000 colon bacilli per dry gram.

tions, Visyneral, neosynephrin, a preparation of zinc, ethylmorphine hydrochloride, vitamins and a low starch diet. The endophthalmitis, headaches, disturbance of vision and depression apparently were benefited more by the vaccine of coliform bacteria than by other remedies.

CASE 4.—Mrs. W. T. D., aged 29, was first examined on April 29, 1938. Her chief complaints were that she was tired after reading and attending the theater and had much burning and other irritation of the eyes. There was a history of sensitivity to sea food, inflammation of the nasal membranes and postnasal discharge. A diagnosis of superficial punctate keratitis was made.

The vision with correction was 20/20 + 2 in the right eye and 20/15 in the left eye.

On July 19, 1939 a culture of nasal secretion showed a moderate number of aerobacters (*A. aerogenes*). A culture of material from the nasopharynx showed *Bacillus pyocyaneus* and *A. aerogenes*. Chronic bilateral hyperplastic ethmoiditis was diagnosed by Dr. F. M. Law and Dr. Otto M. Schmidt.

The patient had recurring attacks of fever with superficial punctate keratitis and retrobulbar neuritis, with great pain from a sphenopalatine ganglion syndrome which had apparently been associated with chronic sinusitis for three years.

She was not benefited by treatment with various local antiseptics, metaphen, autogenous coliform bacteria vaccine, streptococcus and staphylococcus vaccine and sulfanilamide or by Proetz's displacement treatment, colonic irrigations, typhoid inoculations and other nonspecific injections.

She could not tolerate the smallest dose of vaccine of coliform bacteria, streptococci or staphylococci. Her vision decreased to 10/100 in the right eye and 10/30 in the left.

During a prolonged stay in Florida in 1939 the vision improved to 20/50 in the right eye and 20/25 in the left eye coincidentally with improvement in the nasal symptoms and abatement of the fever. When the condition recurred in 1940 treatment was tried in New York for several months before the patient was sent to Phoenix, Ariz., where the condition of the sinuses improved, the temperature became normal and the vision gradually returned to 20/25 in the right eye and 20/20 in the left eye. Immediately on her return to New York the fever recurred, the disease of the sinuses flared up and the eyes became affected. The cultures of nasopharyngeal secretion still revealed *A. aerogenes*.

COMMENT AND SUMMARY

Coliform bacteria isolated from the upper respiratory tract of patients with certain inflammatory diseases of the eye were studied for their possible etiologic role. It had previously been observed that these organisms produced uveitis and were highly pathogenic for the rabbit (particularly for the uveal tissue). Furthermore, it had been observed that coliform bacteria were recovered on repeated cultures from the upper respiratory tracts of many patients with serious inflammation of the uveal tract.

We have been unable to furnish and we have been unable to find statistics on the incidence of coliform bacteria in the upper respiratory tracts of persons presumed to be free from disease. It is obvious that knowledge concerning cultures of material from a group of normal sub-

jects might be of value if it were possible to be sure that the subjects were free from disease.

Since the classification of these bacteria is unsettled, Parr's suggestion has been used, namely that the following organisms be grouped under the term coliform bacteria: the *Klebsiella* genus, *A. aerogenes*, typical and atypical strains of *Esch. coli*, Morgan and paracolon bacilli, *Esch. freundii*, *Shigella*, *Eberthella*, *Salmonella*, *A. cloacae* and *Proteus*.

As many varieties of these organisms were encountered in the upper respiratory tract as in the intestinal tract, though the proportion of mucoid and atypical strains was higher in the upper respiratory tract. Of 120 cultures of exudate from the upper respiratory tract, 29.2 per cent showed typical strains of *Esch. coli* and 70.8 per cent showed atypical strains of *Esch. coli*, paracolon bacilli, *Proteus* or *B. pyocyaneus*. Of 128 fecal strains 62 per cent were typical *Esch. coli* and the remaining 28 per cent were miscellaneous types of coliform bacteria.

With regard to the toxicity of coliform bacteria for animals, the pathogenicity of certain members of this group in diseases of the intestinal tract is well known. Coliform bacteria have been suspected of being the cause of a number of other diseases of animals. Ten Broeck expressed the opinion that they are often secondary invaders which complicate infection and in this way take the place of streptococci in the diseases of man. As early as 1911 Guillery reported that uveitis developed in rabbits from the intravenous injection of filtrates of "ferment-producing" organisms, and in 1916 Woods produced "chronic infiltrative uveitis" with *B. prodigiosus*, an organism somewhat similar to the coliform bacteria.

In previous experiments transitory acute iritis was produced in rabbits by intravenous injection of coliform bacteria recovered from the upper respiratory tract with smaller amounts of culture and with a higher proportion of strains than when other types of bacteria ordinarily found in the upper respiratory tract were used. Bacteria-free filtrates produced the same degree of inflammation as that caused by the original cultures. In general the coliform bacteria isolated from the upper respiratory tract were found to be more lethal and to possess a greater iritis-producing ability for the rabbit than fecal coliform strains.

Except in the case of certain known intestinal pathogens and of acute diseases in which coliform strains have proved to be the causative agent, attempts to establish the pathogenicity of coliform bacteria for man are difficult.

The difficulties in establishing pathogenicity of an organism in individual patients with intraocular inflammation seem to be almost insurmountable at present, and one must depend mainly on clinical and on usual cultural studies, with their lack of certainty in proving a definite etiologic diagnosis. The results of cutaneous tests are believed to bear

little relation to the presence of infection, although they may possibly be used as a quantitative measure of acquired immunity to coliform bacteria, since the reaction tends to diminish with vaccine therapy.

The results of agglutination tests are also of questionable significance. The ability or inability of a patient's serum to agglutinate an autogenous coliform strain seems to give little indication as to its etiologic importance.

The pathogen-selective method is also deemed unsatisfactory for determination of the etiologic importance of coliform bacteria.

Complement fixation reactions lack specificity, even though there is a general positive correlation between the complement-fixing properties of unheated blood serum and the electrophoretic mobility of fecal colon bacilli isolated from the person from whom the blood was obtained. Cross fixation, difficulty in titrating and preserving antigens, variability in anticomplementary properties of different blood specimens and the lack of complement-fixing power of the blood in certain diseases prevented the successful application of complement fixation tests.

Bacteriologic studies of material from one or more suspected foci in the upper respiratory tract were made for 411 patients. Of these, 102 patients harbored coliform bacteria in one or more of the foci; of this group, 68 per cent had some intraocular disease.

Autogenous coliform bacteria vaccines were used in treating certain patients with ocular inflammations associated with the presence of these organisms in the upper respiratory tract. In many instances in which vaccine therapy was associated with partial or complete elimination of coliform bacteria from the upper respiratory tract, there was a noticeable improvement in the general and the ocular condition. Four cases are reported in detail. Nine cases are outlined (table 4) to show the changes in the bacterial flora of the upper respiratory tract in patients undergoing vaccine therapy.

CONCLUSIONS

1. Serious ocular disease is often associated with the presence of coliform bacteria in the upper respiratory tract.
2. Elimination of these microbes from the upper respiratory tract, in which vaccine therapy seemed to be a factor, was associated with improvement and sometimes with cure of certain inflammatory ocular diseases.
3. Coliform bacteria from the upper respiratory tract should be given consideration in the search for possible etiologic agents in some chronic and inflammatory ocular diseases.

Dr. Sidney Rothbard and G. H. Chapman gave constructive criticism.

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ABSTRACT OF DISCUSSION

DR. PETER C. KRONFELD, Chicago: In many instances of uveitis it is impossible to arrive at a definite etiologic diagnosis. Nevertheless, it is the ophthalmologist's duty not to overlook any hint or clue to the proper treatment. This is the idea underlying Dr. Berens' work. At no place in his paper does he claim to have proved the etiologic significance of the coliform bacteria recovered from the upper respiratory tracts of his patients. He has, however, presented evidence that the ophthalmologist should include a search for such micro-organisms in the treatment of patients with chronic uveitis.

The group of cases presented by Dr. Berens appears at first glance rather heterogeneous. Three cases were of chronic or recurrent retrobulbar neuritis with definite sinus disease. To take measures against characteristic micro-organisms recovered from the nose in such cases appears to be a sound clinical procedure.

Dr. Berens' series contains 4 cases of chronic uveitis of a type that practically always presents serious diagnostic and therapeutic problems. The patients seem to have derived definite benefit from the treatment with a vaccine prepared from coliform micro-organisms, a benefit which appears to have been greater than that from any other form of treatment.

Dr. Berens has pointed out a new and promising way of treating chronic ocular inflammation. It is to be hoped that this first small series of cases will soon be followed by a larger and more homogeneous series.

DR. JOHN A. TOOMEY, Cleveland: Many patients ill with ocular infections are admitted to contagious disease hospitals, and many patients already in such hospitals acquire ocular infections of various kinds. Therefore, the underlying cause—whether viral or bacterial—is important to persons working with communicable diseases.

Dr. Berens has been interested in the effect coliform organisms have on uveal tissue. He has often found typical *Esch. coli* organisms in the upper respiratory tract, and he has tried to demonstrate that these are more toxic than the fecal strains of the same organism. Perhaps the activity of the latter had been modified by some phage activity, which is apt to be present in material from fecal sources.

The coliform bacteria mentioned by Dr. Berens cause diseases in animals, such as mouse typhoid, scours, etc. Years ago Ecker, Goldblatt and Biskind demonstrated the pathogenicity of enteric organism filtrates. It is interesting to note that ocular conditions may be caused by such filtrates, although I imagine Dr. Berens would not want to state that an etiologic association has been definitely proved.

I have not identified every gram-negative organism found in the routine cultures of material taken from the nose and throat in the institution with which I am associated, but practically all such cultures show coliform organisms. I wonder whether it is possible ever to render the nose and throat free from *Esch. coli*. I agree with Dr. Berens' estimation of the value of the history as it pertains to the skin, of agglutination tests and of complement fixation tests. Immunologic therapy is difficult to evaluate, even though the results in some patients are striking.

Many years ago I was able to isolate coliform bacteria as well as other organisms from the nares and throats of patients with asthma of bacterial origin. Individual cultures of each bacterium were made

in dextrose broth; the growth was filtered through a W filter, scraped away and killed, and the organisms were saved. It was found that intradermal injection of the filtrate always caused more positive reactions than injection of a suspension of the dead organisms and that a combination of the flora and the filtrate gave a still greater reaction than the filtrate of the individual organism. When the combined flora antigen vaccines were first used they caused an attack of the specific disease, i. e. asthma. This was Dr. Berens' experience, too, but in his case the specific disease was uveitis.

Has Dr. Berens had any comparable results with typhoid fever vaccine?

DR. CONRAD BERENS, New York: I appreciate the discussion and am delighted that Dr. Kronfeld has emphasized the point that we do not believe this paper proves the etiologic significance of coliform bacteria in diseases of the eye.

He has also pointed out even more clearly than we have that apparently there is a striking association between the improvement in the ocular condition and the change in the type of organism found, in the way that this organism would affect animals and the patient's general improvement. We tried all accepted forms of treatment: chemotherapy. the use of grenz rays, roentgen therapy and many other measures. Naturally vitamins had to be considered in these days of a vitamin "cure" for every disease.

We often used inoculations with typhoid fever vaccine, mentioned by Dr. Toomey, and 1 patient with retrobulbar neuritis had been given several courses of typhoid fever therapy without apparent benefit before we treated her.

RETINAL PHLEBOSCLEROSIS

GLEN GREGORY GIBSON, M.D.

AND

LAWRENCE W. SMITH, M.D.

PHILADELPHIA

It is our impression that during the past few years we have been encountering more patients in whom we can observe changes which suggest sclerosis of the retinal veins. Attempts to classify these changes adequately have been difficult because material for a combined ophthalmoscopic and microscopic study is rarely available. In this paper we have attempted to approach the problem of the classification of retinal phlebosclerosis, combining clinical and microscopic evidence, although to some extent it has been necessary to rely on inference rather than on proof.

In view of the fact that the venous changes to which we refer resemble in some ways the changes observed in retinal arteriosclerosis, we have assumed that they are due to retinal phlebosclerosis. The rather frequent observation of venous sclerosis in microscopic retinal sections makes this assumption somewhat more justifiable. That the venous and the arterial lesions do not appear identical is evident for anatomic, physiologic and pathologic reasons. Since retinal phlebosclerosis is rather rare and since it does not have the diagnostic significance associated with retinal arteriolar sclerosis, it has received relatively little consideration in the literature. Recently O'Brien and Allen¹ called attention to venous sclerosis in association with diabetes, and they and their discussers expressed a desire for more work on the unsettled relation between the two conditions.

TYPES

The three main types of retinal venous lesions which we have encountered and have classified as phlebosclerosis, as seen ophthalmoscopically, are dependent on whether the process is initiated within the lumen, within the wall or outside the wall of the vein. Lesions in which the process starts within the lumen are classified as the intimal type and are recognized only after venous thrombosis and fibrosis have occurred. Lesions

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Read before the Section on Ophthalmology at the Ninety-Second Annual Session of the American Medical Association, Cleveland, June 4, 1941.

1. O'Brien, C. S., and Allen, J. H.: Unusual Changes in the Retinal Veins, *Arch. Ophth.* **24**:742 (Oct.) 1940.

of the medial type are recognized when the sclerotic process in the wall of the vein becomes sufficiently severe to produce indentations in the lumen and changes in the contour of the vein. Lesions of the adventitial type are recognized after the subsidence of perivenous inflammation or edema, when resultant connective tissue ensheathes the vein.

DESCRIPTION

The intimal type of sclerosis occurs after thrombosis in veins in which the circulation is not reestablished. The vein appears white and fibrous peripheral to the thrombosis. The contour of the vein, however, is smooth (fig. 1 *A*). The minimal degree of the medial type of sclerosis appears as a slight beading of the vein. There are usually numerous not quite regularly spaced indentations, or constrictions, of the venous



Fig. 1.—*A*, post-thrombotic intimal sclerosis associated with hypertension. The patient had cardiovascular-renal disease. (From Smith, L. W.; Weiss, E.; Lillie, W. I.; Konzelmann, F. W., and Gault, E. S.: Cardiovascular-Renal Disease, New York, D. Appleton-Century Company, Inc., 1940.) *B*, early medial venous sclerosis associated with diabetes in a nonhypertensive patient. The condition progressed to complete occlusion of all the veins.

wall which encroach slightly on the normal lumen of the vein. Between these focal constrictions are areas of slight dilatation. At this stage it is unusual to find evidence of venous obstruction, such as hemorrhages or exudate (fig. 1 *B*).

In the more advanced stages the beading becomes obvious and the course of the vein is deflected to produce sharp-angled kinks and tortuosities (fig. 2). Occasionally the venous wall becomes visibly thickened. Disturbances of circulation are the rule with this degree of involvement, and thrombosis, infarction, fibrosis and thickening of the retina may be encountered subsequently. Unlike the intimal type, which is

usually limited to one vein, the medial type frequently involves all the retinal veins. However, in a case of bilateral diabetic retinopathy, advanced retinal phlebosclerosis was present in all the veins of one eye, and the veins in the other eye were grossly normal.

The adventitial, or secondary, type of phlebosclerosis (fig. 3) is produced by perivenous inflammation or edema, and there is usually residual evidence of this to assist in the diagnosis. The venous changes are usually limited to the area of inflammation and are characterized by a white connective tissue sheath around the vein.

Two of our patients, a woman of 27 (fig. 1 *B*) and a man of 31, each of whom had a family history of diabetes, was known to have had diabetes for several years and needed less than 25 units of insulin daily, presented early bilateral retinal phlebosclerosis. In spite of extensive

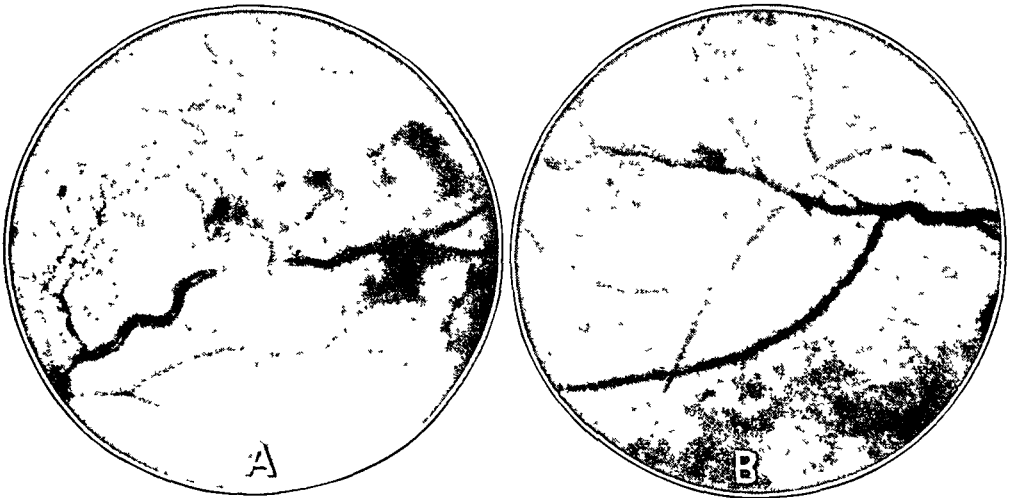


Fig. 2.—*A*, medial venous sclerosis and diabetic retinopathy associated with hypertension. *B*, medial venous sclerosis and diabetic retinopathy associated with hypertension.

diagnostic and therapeutic procedures the veins became progressively sclerosed, producing multiple thrombi and hemorrhages in the retina. Later bilateral massive hemorrhage of the vitreous occurred. A year later the hemorrhages had been absorbed but the sclerosis persisted, the retinas were extremely thickened and detachment of the retina had occurred in the man and severe secondary glaucoma in the woman. These patients had slowly progressive retinal phlebosclerosis of the medial type terminating in complete loss of the visual function.

INCIDENCE

Retinal phlebosclerosis is relatively rare. Most patients with hypertensive or diabetic retinopathy do not show evidence of this condition. Frequently the changes are so mild that unless one is searching for the

condition it is easily overlooked. We have estimated that in the past five years we have noted about 20 cases in which sclerosis of the veins was suspected or diagnosed.

ETIOLOGY

The causation of venous sclerosis has much in common with that of arterial sclerosis and likewise is somewhat obscure. It seems fair to conclude that the intimal type of venous sclerosis, which is usually associated with chronic hypertensive arteriosclerosis, has a similar causation. More rarely it accompanies thromboangiitis obliterans, as reported by Wagener,² or follows endophlebitis obliterans, as reported by Verhoeff.³

We have seen the most advanced degree as well as the most progressive form of the medial type of venous sclerosis in patients who had diabetes mellitus. Patients in whom both diabetes and hypertension



Fig. 3.—Adventitial type of venous sclerosis (postinflammatory).

are present seem to be more prone to acquire sclerosis of the retinal veins. The role of diabetes and that of venous disease were discussed and the venous lesions of diabetes described by Wagener, Dry and Wilder⁴ in 1934. It is our impression that the medial type of venous disease associated with diabetes is metabolic in origin and is not produced by the retinopathy. That this venous disease, however, may lead to retinitis proliferans has been pointed out. In all the retinal veins in the affected eye of a young woman who had a traumatic arteriovenous

2. Wagener, H. P.: Differential Diagnosis and Types of Retinitis, Instructional Course of American Academy of Ophthalmology and Otolaryngology, Chicago, October 1939.

3. Verhoeff, F. H.: Obstruction of Central Retinal Vein, *Arch. Ophth.* **36**:1, 1907.

4. Wagener, H. P.; Dry, T. J., and Wilder, R. M.: Retinitis in Diabetes, *New England J. Med.* **211**:1131, 1934.

aneurysm between the common carotid artery and the cavernous sinus we observed a marked medial sclerosis which was probably due to the resultant increased intravenous pressure.

To some extent it is the duration of the disease and not the age of the patient which determines the presence of phlebosclerosis. Most writers on diabetic retinitis express the opinion that there exists a similar relation between the retinitis and the duration of the diabetes. It is suggested that further study on the causes of venous sclerosis may be of some assistance in the study of the causes of arteriosclerosis.

DIFFERENTIAL DIAGNOSIS

Several conditions have to be differentiated from true phlebosclerosis. The first of these is the presence of excess glial tissue around the disk. Such gliosis is not restricted to the perivenous tissues but is found likewise around the arteries. The gliosis is most marked at the disk, produces no vascular deformity, has a characteristic waxy appearance and diminishes in amount along the vessels progressively from the disk toward the periphery of the fundus.

Another condition which warrants mention is the presence of congenitally atypical veins. These may be recognized by their larger size, their atypical distribution and their anomalous branching pattern. Sometimes they are beaded, but they are never associated with circulatory disturbance in spite of such obvious abnormalities. An anomalous arterial tree usually accompanies congenitally atypical veins.

Another condition, described by Edward Thomas,⁵ which has to be differentiated is the slight venous beading frequently produced peripheral to a partial occlusion of the vein by an arteriosclerotic artery at the point of arteriovenous crossing. It is also necessary to differentiate the beading and the perivenous leukocytic infiltrates of leukemia, which simulates phlebosclerosis.

PATHOLOGY

O'Brien and Allen,¹ discussing the retinal venous changes associated with diabetes, commented on the occasional occurrence of beaded varicosities in patients with long-standing, poorly controlled diabetes and arteriosclerosis. One of their patients, a man aged 65 with a fifteen year history of diabetes, had a blood sugar content of 447 mg. per hundred cubic centimeters and a blood pressure of 170 systolic and 110 diastolic. At autopsy sclerosis of the retinal veins was observed, with variations in the thickening of the walls corresponding to the beading of the veins noted clinically with the ophthalmoscope. This was in addition to advanced arterial lesions and the changes of typical diabetic retinitis.

5. Thomas, E., in discussion on O'Brien and Allen.¹

Agatston⁶ in a preliminary report confirmed the existence of sclerotic venous lesions and of their frequency in diabetic persons. He described fibrosis of the intima, with separation of the longitudinally directed fibrils and even complete hyalinization of the walls. The process, he noted, extends to involve the venules and the capillaries.

Retinal material for microscopic proof of our clinical diagnoses has not been available; however, through the courtesy of the Army Medical Museum we have had an opportunity to study sections of the retina from 7 diabetic patients. Definite sclerotic changes in the retinal veins of one of the specimens can be demonstrated. Earlier changes of the medial type are fairly well established in a second. No phlebosclerotic changes are present in the other 5. Under the microscope, in the constricted areas the veins show proliferation of the lining endothelial cells, thickening of the wall and a variable amount of accompanying hyaline degeneration. In several places degeneration of the lining endothelium suggests some circulating toxic agent as a probable etiologic factor. O'Brien and Allen¹ and Agatston⁶ have made the same comment, Agatston suggesting that "while the presence of hyperglycemia may be responsible for metabolic changes in arterial walls, the effect is even more specific on capillaries and veins."

In this connection it is interesting that the most marked retinal phlebosclerosis seems to occur in cases of rather mild, long-standing diabetes rather than in cases in which the blood sugar content is especially high. This suggests that it is not the hyperglycemia which is responsible for the vascular changes but rather an alteration in some other metabolic product resulting from the disturbance in carbohydrate metabolism.

In addition to the 7 retinal specimens from persons with diabetic retinitis, we have studied 100 microscopic retinal specimens from the collection of the Army Medical Museum. These represent a fair cross section of ophthalmic disease. Ninety-six are entirely negative so far as the medial type of phlebosclerosis is concerned. However, several show venous lesions in association with extramural disease of various kinds, including the dilatation accompanying leukemic infiltration and hemorrhages related to retinitis of different types.

In the remaining 4 specimens varying degrees of the medial type of phlebosclerosis were found. Two of the cases are listed as instances of diabetes, and on checking against the 7 previously studied retinal specimens from diabetic persons we found that 1 (no. 40413) was duplicated in the loan collection. Thus, of a total of 8 retinas from persons known to be diabetic, 2, or 25 per cent, show demonstrable

6. Agatston, S. A.: Clinicopathologic Study of Diabetic Retinitis, *Arch. Ophth.* 24:252 (Aug.) 1940.

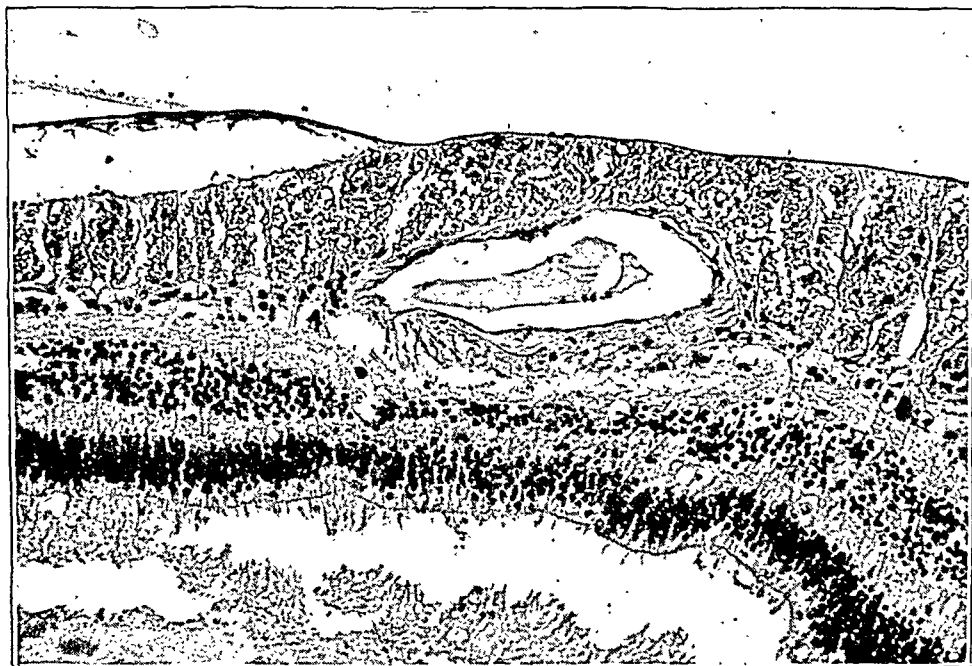


Fig. 4.—Medial retinal phlebosclerosis associated with diabetes.

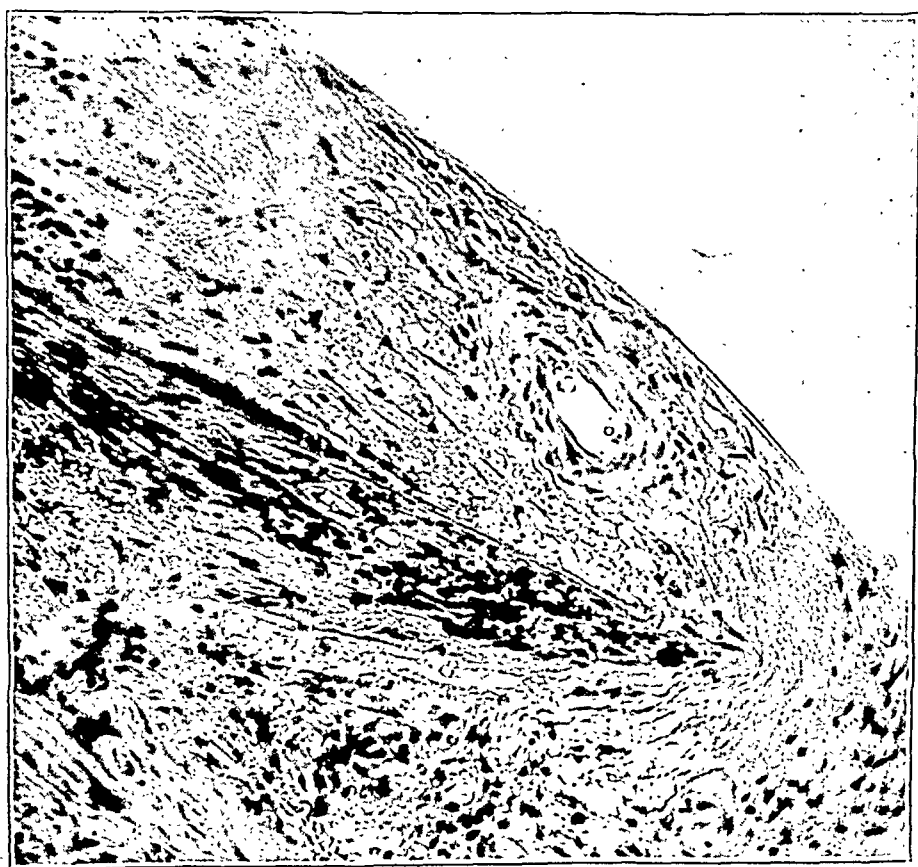


Fig. 5.—Mild retinal phlebosclerosis associated with diabetes.

venous sclerotic lesions. The third specimen is from a hypertensive patient who had shown in addition to the phlebosclerosis moderately advanced arteriolar sclerosis. The fourth is from a 70 year old man with chronic glaucoma who had had an iridectomy shortly before death. The venous changes are minimal, and the picture is complicated by a thrombus of the retinal vein.

Finally, we had the opportunity of studying at autopsy the retina of a 50 year old hypertensive woman with mild diabetes. During the last few months of life she had had malignant hypertension as the acute, terminal phase of long-standing hypertension, with a blood pressure

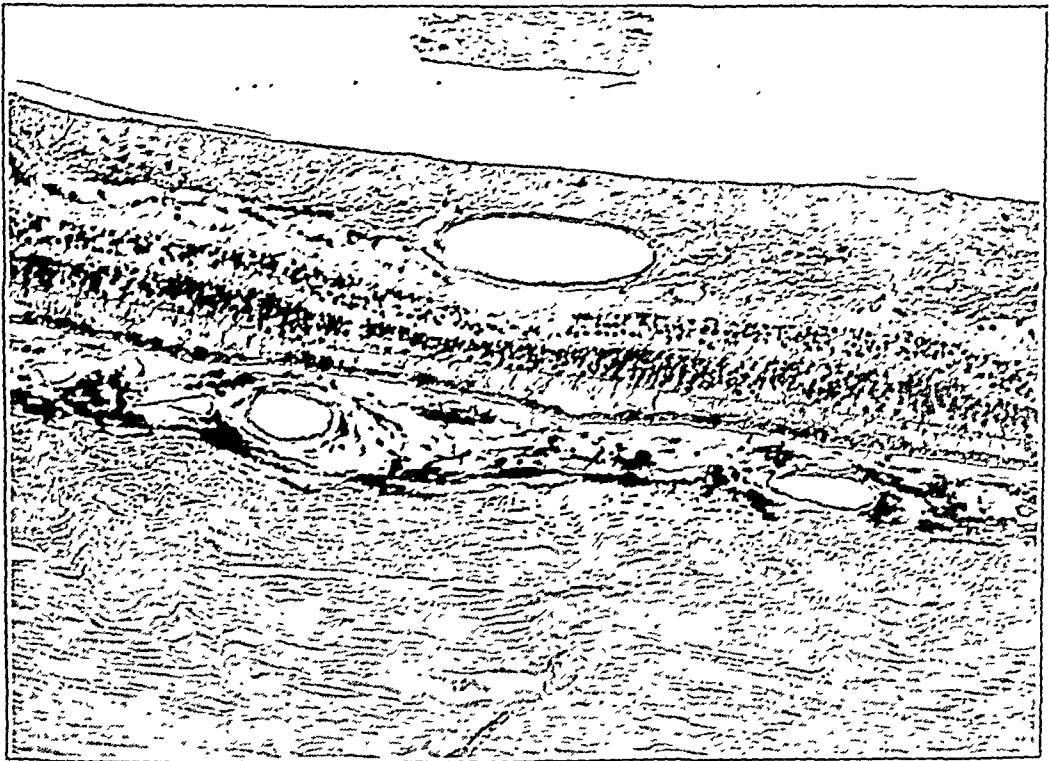


Fig. 6.—Retinal phlebosclerosis associated with hypertension and diabetes.

averaging 250 systolic and 150 diastolic. On her admission to the hospital the sugar content was 165 mg., the urea content 86 mg. and the creatinine content 14.6 mg. per hundred cubic centimeters of blood. Autopsy revealed a heart with typical concentric ventricular hypertrophy on the left, small red granular kidneys and a small fibrotic pancreas. Microscopically the diagnosis of malignant nephrosclerosis was established through the presence of hyaline necrosis of the glomerular arterioles and typical hyperplastic arteriolar sclerosis. In the pancreas, many of the islands of Langerhans were partially hyalinized and fibrosed.

Sections of one eye revealed advanced disease of the retinal arterioles. In addition, moderate phlebosclerosis of the medial type was

found. In this case the phlebosclerosis should be interpreted perhaps as having developed as a result of a combination of the hypertensive and the diabetic processes.

We wished to study veins from other organs and tissues of diabetic persons to see whether medial sclerosis occurs with significant frequency elsewhere than in the eye. Accordingly we reviewed autopsy tissue from 3 diabetic persons. No lesions of corresponding magnitude were noted, although occasional veins were encountered which might be considered to show the type of pathologic change under discussion. Warren⁷ in his monograph on the pathology of diabetes mentioned no

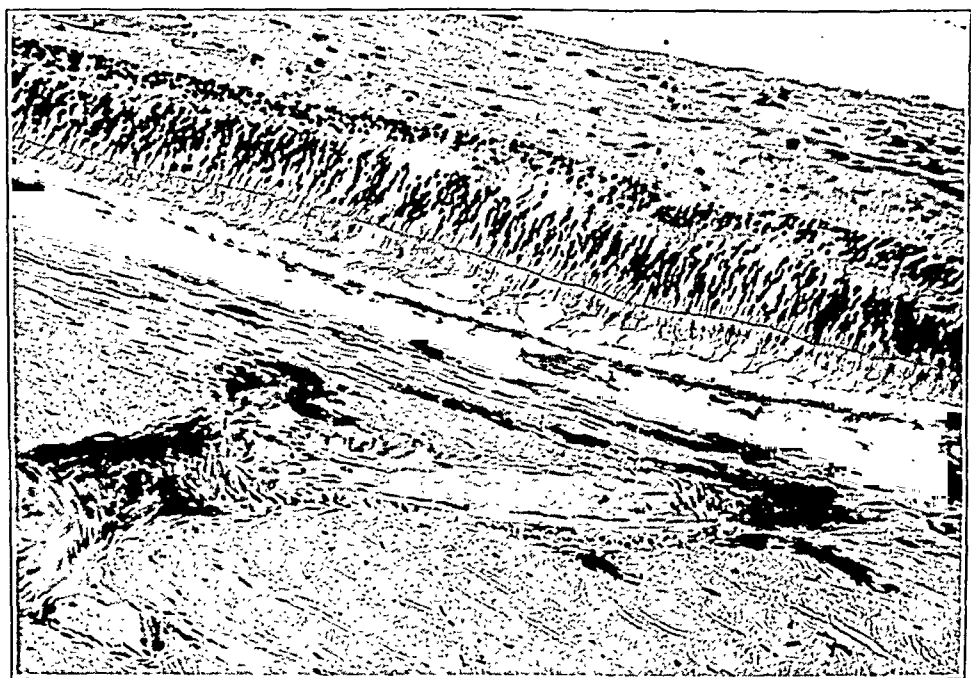


Fig. 7.—Sclerosis of the vortex vein in a patient with severe hypertension, mild diabetes and severe glaucoma.

venous disease except a secondary phlebitis and lymphangitis resulting from the extension of the gangrenous process accompanying arterial disease in the extremities.

SIGNIFICANCE

Retinal phlebosclerosis is of some diagnostic significance in occasional cases of diabetes, arteriosclerosis, thromboangiitis obliterans and retinal inflammation. We are under the impression that it is increasing in frequency because of the longer life of the diabetic person today.

7. Warren, S.: *The Pathology of Diabetes*, ed. 2, Philadelphia, Lea & Febiger, 1938.

Ordinarily it runs a mild, chronic and slowly progressive course. Occasionally, however, especially in some young diabetic patients and some patients with slowly progressive hypertensive disease, the phlebosclerotic process progresses to the point of total venous occlusion. This may develop over a period of six months to a year and be followed by complete infarction of the retina with complete loss of vision. Such progressive mural venous sclerosis obviously has serious significance.'

SUMMARY

The increasing incidence of retinal phlebosclerosis as a complication of diabetes is commented on. A classification of the various types of this venous lesion is proposed, their causation discussed and a description of each given. The differential diagnosis and the pathologic changes in the retinas of 107 eyes are discussed. The literature on this condition is reviewed briefly, and the clinical significance of the picture is pointed out.

ABSTRACT OF DISCUSSION

DR. CECIL S. O'BRIEN, Iowa City: I should like to take this opportunity to express my gratitude as a student of Dr. Zentmayer, whom I consider one of my two great teachers.

One is always pleased to have one's findings corroborated, and Dr. Gibson and Dr. Smith's paper and Dr. Agatston's paper both confirm the findings which Dr. Allen and I expressed before this section last year, namely that in a great number of persons with diabetes, particularly those with the mild, long-standing type, there are notable changes in the retinal veins and these, as we proved to our satisfaction last year by section of an affected eye, are due to sclerotic changes.

It seems strange that so little mention has been made of pathologic changes in the retinal veins associated with diabetes and arteriosclerosis. Perhaps the explanation of these changes, or of the more frequent finding of them now, lies in the fact that diabetic persons live a great deal longer than they formerly did. Perhaps the changes are due to toxic or metabolic causes, and perhaps they come only with long-standing diabetes.

It seems to me almost the rule to find arteriosclerosis in diabetic patients who have had the disease for any length of time. Even in some younger diabetic persons Dr. Allen and I have been able to find arteriosclerotic changes, and certainly it must be unusual not to find more or less advanced sclerotic changes in the arteries in older patients. Consequently one would expect that the toxins or the metabolic by-products would affect not only the arteries but the veins and probably the capillaries as well.

The 21 patients on whom Dr. Allen and I reported before this section all had long-standing, mild diabetes. We found in the venous walls many changes such as those reported by Dr. Gibson and by Dr. Smith. We found hyaline degeneration of the venous walls, variation in the thickness of the walls, dilatations or varicosities in certain places, con-

strictions in other places and all the endothelial proliferations and other changes which one might expect in degeneration of the walls of the veins.

DR. HENRY P. WAGENER, Rochester, Minn.: In many instances in which a vein crosses, is crossed by or lies in close approximation to a severely sclerosed arteriole, thickening of the wall of the vein can be demonstrated histologically. According to Koyanagi this thickening is largely in the adventitia, especially when the arteriole and the vein are enclosed in the same sheath. At times some irregularity in the lumen of the vein distal to the point of actual compression is observed ophthalmoscopically. I have been accustomed to consider this irregularity as evidence of phlebosclerosis. It may represent mural thrombosis, since I have occasionally observed after an interval of six months or a year complete thrombosis of the vein at this point. At times, also, a localized narrowing is present in the lumen of a vein which is not in close association with a sclerosed arteriole. I have assumed that this narrowing is due to sclerosis of the wall of the vein, though I do not have any histologic proof for this assumption.

The involvement of the retinal veins seen in association with diabetes mellitus differs ophthalmoscopically, in my opinion, from that seen with any other disease. The three outstanding features seem to be (1) the nodular dilatations stressed both by Gibson and Smith and by O'Brien and Allen in their paper before this section last year; (2) the tendency to venous capillary proliferation, to which scant attention has apparently been paid, and (3) the deposition or accumulation of yellowish white material under or around localized sections of individual veins.

From the standpoint of ophthalmoscopic appearance it is difficult to believe that the wall of the vein is sclerosed in the areas of nodular and at times fusiform dilatation. Rather, the wall appears to be softened or at least to have become more permeable than normal, since blood seems to ooze directly from some of these dilated sections. I wonder whether the thickening of the walls of the veins demonstrated histologically by Gibson and Smith and by O'Brien and Allen may be more like the thickening of the capillary basement membrane of the glomerular tufts which permits increased escape of albumin in cases of nephrosis than the typical medial hypertrophy of arteriolosclerosis. The suggestion that mural thrombosis may be the cause of the peculiar ophthalmoscopic appearance of the veins has not received definite histologic confirmation. Apparently the anatomic or histologic nature of the peculiar loop formations noted in many of the veins has not been demonstrated definitely.

The tendency to proliferation of new vessels, in the main of capillaries but at times of those of larger size, has seemed to me to be a striking feature of retinal venous disease in cases of diabetes. The new vessels develop apparently from a retinal vein, at times on the disk but often also in peripheral parts of the retina. Their location does not always correspond to the nodular dilatations in the veins, and they may develop in retinas in which nodular venous dilatations are not present and in which there is no visible arteriolosclerosis. They occur frequently without evidence of massive bleeding into the retina or the vitreous, although when they are seen small punctate hemorrhages are scattered, usually in the retina. During the first stages of their development they are not associated with any visible evidence of connective tissue proliferation. Later

delicate strands, or membranes, of connective tissue are seen in association with the newly formed vessels. It is my impression that some of the recurrent bleeding into the vitreous in diabetic patients occurs from these delicate newly formed vessels.

In 1938 Bertha Klien (*Retinitis Proliferans*, *Arch. Ophth.* 20:427 [Sept.] 1938) called attention to two types of retinitis proliferans, one in which "the formation of connective tissue precedes the formation of new blood vessels" and another in which "there is a primary formation of new vessels with secondary production of a scaffolding of delicate connective tissue." She expressed the opinion that in the second type the proliferation is consequent to "a slow circulatory impairment due to degenerative vascular disease with the formation of new compensating anastomotic channels, with or without hemorrhage at first." She stated that this type is found often in association with diabetes and presented drawings illustrating it in a patient 46 years of age who had had diabetes for four years and whose blood pressure was normal. It would be interesting to know the basic nature of the disease of the veins which leads to vascular proliferation of this type.

The exact nature and the origin of the yellowish white material seen along the margins of, or perhaps underlying, certain sections of the veins in cases of advanced retinitis of the diabetic type have not been entirely clear to me. Occasionally a similar deposit is observed along an isolated arteriole in the same retina. O'Brien and Allen called this appearance evidence of sclerosis. I am rather inclined to agree with Gibson and Smith's opinion that it represents coagulated exudate in the perivenous (and periarteriolar) spaces. It is certainly in no sense equivalent to the periarteriolar sheathing seen ordinarily in association with arteriolo-sclerosis of the hypertensive type.

On the whole, then, the histologic changes described to date in the veins of the retina do not seem to be sufficiently severe or characteristic to account for the extensive changes observed ophthalmoscopically in cases of diabetic retinitis. Unless it is to be assumed that there exists some metabolic tissue change which cannot be demonstrated histologically, it would seem that more intensive studies of more specimens will be necessary to reveal the exact nature of the lesions. It is difficult to obtain eyes for microscopic examination, especially eyes in the early phases of diabetic retinitis. Drs. Gibson and Smith deserve considerable credit for their intensive search for material. Undoubtedly their studies are a step toward the proper classification of lesions of the retinal veins to which pathologists have paid so little attention in the past.

DR. GLEN GREGORY GIBSON, Philadelphia: I wish to thank the discussers for their kind consideration. Dr. Smith and I are particularly fortunate in having had Dr. Wagener discuss our paper, because he has pointed out its shortcomings. He was good enough to show me his discussion before the session convened and to ask me if there was anything I should like to have stricken out as too critical. Since our objective is the truth, I told him to give it exactly as he had it, and I am indebted to him for pointing out the truth about the situation.

We have not proved that these lesions are actually due to the phlebosclerosis. They seem to be due to that, but the actual proof is yet to be brought forth.

OPHTHALMIC ZINC SULFATE SOLUTIONS

BUFFERED, ISOTONIC AND PRESERVED

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Zinc sulfate solutions in varying concentrations have been used in the practice of ophthalmology for many years. However, in spite of their long popularity as ophthalmic medicaments, almost all such solutions as ordinarily dispensed have two disadvantages. First, they are irritating to the delicate corneal tissues and, as a result, produce excessive lacrimation. This condition causes the active ingredients to be washed from the eye, thus greatly decreasing the therapeutic effectiveness of the zinc sulfate. Secondly, most of the preparations are dispensed unpreserved and contain zinc sulfate in combination with boric acid—a mixture which constitutes an admirable medium for the growth of microorganisms such as yeasts and molds.¹

We have undertaken the present study in an effort to produce non-irritating and preserved zinc sulfate solutions which will lend themselves to more effective medication of the eyes than most such solutions now in common use. The adjustments made on ordinary ophthalmic preparations of zinc sulfate to compensate for the disadvantages mentioned are discussed in the following paragraphs.

PRESERVATION

The preservation of ophthalmic solutions against the growth of microorganisms such as yeasts and molds is not easily achieved. The ordinary methods of sterilization are both impractical and difficult to apply. For example, many ophthalmic preparations cannot be sterilized by heat, since this would destroy the active ingredients; moreover, as with most physical methods of sterilization, the solutions would stay sterile only

1. Skauen, D. M., and Burroughs, G. L.: *Pharm. Arch.* **2**:72, 1940.

as long as they remained free from exposure to contamination. Consequently, the most desirable and effective method of sterilization is the addition of a physiologically inert, nonirritating, bactericidal and fungicidal agent which is compatible with the active ingredients. With this method the sterility will be maintained even though the solution is exposed to contamination by micro-organisms.

We investigated several of the esters of parahydroxybenzoic acid for their preservative qualities. Agar plates containing nutrient medium treated with various concentrations of the several preservatives, along with an untreated control, were inoculated with a uniform emulsion of the micro-organisms found growing in an unpreserved collyrium. The results obtained on twenty-four hour cultures are listed in the accompanying table.

Preservative Qualities of Several Parahydroxybenzoic Acid Esters

Ester of Parahy- droxy- benzoic Acid	Concentration in Percentage											
	0.01	0.015	0.02	0.025	0.03	0.04	0.05	0.08	0.1	0.15	0.2	Control
Methyl	+++	—	..	++++
Ethyl	+++	++	—	++++
Propyl	+++	..	—	—	++++
Butyl	+++	++	—	++++
Mixture of methyl 65 parts and propyl 25 parts.....	++	—	..	—	++++

The preservative qualities of the methyl, ethyl and propyl esters were in accord with those noted by Sabalitschka and Böhm² except that in all cases our results showed that lower concentrations of the preservatives are effective in preventing the growth of micro-organisms. This in all probability can be attributed to the fact that the mixture of micro-organisms used to inoculate the agar plates was not identical in the two studies.

The results shown in the table indicate that butyl-p-hydroxybenzoate is the most suitable preservative of the compounds investigated and that the propyl, methyl and ethyl esters are effective in that order. On further investigation of these compounds it was discovered that the butyl and ethyl esters produced noticeable irritation when applied to the eyes, and they were discarded from this standpoint. The propyl ester produced only slight irritation, while the methyl ester was found to be nonirritating.

2. Sabalitschka, T., and Böhm, E.: *Zentralbl. f. Bakt. (Abt. 1)* **123**:351, 1932.

In order to have a preservative which would be nonirritating and still effective in low concentration, we investigated several combinations of the methyl and propyl esters. The combination finally selected was the same as that used by Hasler³ and consisted of 65 parts of methyl-p-hydroxybenzoate and 35 parts of propyl-p-hydroxybenzoate. This mixture in 0.04 per cent concentration was found to prevent the growth of micro-organisms and was adopted as the most desirable preservative for the zinc sulfate ophthalmic preparations to be described.

TONUS AND ITS RELATION TO OPHTHALMIC SOLUTIONS

A solution is said to be isotonic when it exerts exactly the same osmotic pressure as a second fluid with which it is brought in contact. Whenever a solution is applied to the eye, unless it is of the same osmotic pressure as, or is isotonic with, the tears, a sharp and painful irritation will be created.

If a hypotonic solution is applied to the eye the tissue fluids will absorb water from it, thus causing the cells to become engorged with fluid—a condition which causes painful reactions. If the collyrium is hypertonic it will withdraw water from the tissue fluids until an equilibrium is established at the point at which the osmotic pressures of the two solutions are equal. This withdrawal of water causes dehydration and shriveling of the tissues, which in turn produce painful reflexes.

It can be readily seen from these facts that an isotonic solution would be much more efficient and desirable in treating the eyes than one whose osmotic pressure had to be readjusted by the absorption of water from the tissue fluids, as in the case of hypertonic solutions, or by the loss of water to the tissue fluids, as in the case of hypotonic solutions.

BUFFER ACTION AND ITS APPLICATION TO COLLYRIUMS

Not only must the tonus of a solution to be used in the eye be adjusted, but the reaction, or p_H , must be adjusted so that it is within the narrow limits of that of the lacrimal fluid if a completely nonirritating and effective collyrium is to be prepared. Not only must the p_H of the solution be made to approximate that of the tears, but it must be adjusted so that it will remain at that level with only very small deviations. This is accomplished by the addition of buffer salts to the collyrium. Although the normal p_H of the lacrimal fluid is about 7.4, we have found that if an ophthalmic solution is within the p_H range of about 6.5 to 7.8 it is relatively nonirritating provided it is also isotonic with the tears.

3. Hasler, W. T.: *Am. J. Ophth.* **22**:423, 1930.

Buffer action is defined as the ability of certain salts when dissolved in water to resist a change in p_H on the addition of a small amount of acid or base. The term buffer salt is applied both to the salts of weak acids, such as phosphoric and acetic acid, and to the salts of weak bases.

The principle of buffer action when a buffer solution is added to a second solution containing a small amount of acid or base can be explained as follows: The addition of an amount of buffer salt relatively large in proportion to the amount of acid or base present causes a fractional decrease of the buffer ion through its union with the hydrogen ion to form the slightly dissociated acid corresponding to the buffer salt employed. The decrease in the amount of buffer salt will then be so slight that the hydrogen ion concentration will remain practically constant.

The application of this principle of buffered solutions of collyriums has become increasingly important as the knowledge of the reaction of the lacrimal fluid and its effect in the therapy of the eye for various pathologic conditions has increased. For example, it is well established that pneumococcic organisms cannot live at a p_H of less than 7.0 and consequently should be treated with an acid collyrium. Streptococci, on the other hand, require an alkaline medium for efficient treatment.⁴

In general terms, it may be said that conditions causing acidity in the eye should be treated with an alkaline collyrium, and vice versa. Thus, the corneal injury is treated with an acid solution because it produces an alkaline fluid about p_H 8.4, which should be compensated for. However, it is not sufficient merely to apply a simple alkaline or acid solution to the eye, as required, because the extreme reaction of the lacrimal fluid will neutralize the collyrium and quickly return the reaction to the original level.

To remove the possibility of having an uncontrolled reaction of the lacrimal fluid during the therapy of pathologic conditions of the eye, the use of buffered collyriums has been evolved. A buffered solution of the proper p_H for the pathologic condition will immediately bring the p_H of the lacrimal fluid to approximately that of the buffer and prevent any change in p_H as long as it remains in the eye.

In several cases we found that the lacrimal fluid did not change the p_H of a well buffered solution more than 0.1 of a p_H unit; therefore a p_H of 6.75 was adopted as desirable for ophthalmic solutions except when a streptococcic infection is being treated or when a salt that is soluble only in an alkaline solution is used.

4. Hosford, G. N., and Hicks, A. M.: Hydrogen Ion Concentration of Tears: Its Relation to Certain Ocular Symptoms and to Conjunctival and Corneal Lesions, *Arch. Ophth.* **13**:14 (Jan.) 1935.

PREPARATION

From the facts mentioned in the foregoing paragraphs, it can be readily seen that most of the irritating properties of ordinary ophthalmic preparations are due to the fact that the preparations are not buffered to the p_H range which is consistent with comfort or made isotonic with the lacrimal fluid. In many of the ophthalmic solutions on the market one of these factors is compensated for, but with very few have both been taken into consideration, a condition which leads to only a partial elimination of the irritant properties.

In the preparation of our new zinc sulfate ophthalmic solutions, we adjusted both the reaction and the tonus of each solution, thus making it nonirritating in both the 0.125 per cent and the 0.25 per cent concentrations. The p_H of the solution was adjusted to 6.75, which is well within the range of comfort, and the tonicity was adjusted to correspond with that of the tears.

To obtain a solution having a p_H of 6.75, two buffer solutions were prepared, an alkaline solution containing sodium acetate and zinc sulfate and an acid solution containing boric acid and zinc sulfate. Both were made isotonic with potassium chloride. The two solutions were mixed in the proportions necessary to make the final p_H 6.75.

The most convenient and accurate method for the calculation of the amounts of salts necessary for an isotonic collyrium takes into consideration besides the isotonic factor of the lacrimal fluid the concentration of the salts and their molecular weights and ionization factors. The following formula, based on the work by Nicola,⁵ was used in the preparation of the isotonic zinc sulfate solutions.

$$\begin{array}{c}
 \text{0.04307} \\
 \text{(Isotonic factor} \\
 \text{of lacrimal} \\
 \text{fluid)}
 \end{array}
 - \frac{\text{Percentage of} \\
 \text{active ingredient} \\
 \text{in solution}}{\text{Molecular weight of active} \\
 \text{ingredient in solution}} \times \text{Ionization factor} \\
 \text{of active ingredient} \\
 \\
 \times \frac{\text{Molecular weight of salt to} \\
 \text{be used to make} \\
 \text{solution isotonic}}{\text{Ionization factor} \\
 \text{of salt to be used to} \\
 \text{make solution isotonic}} = \text{Number of grams of salt} \\
 \text{used to make solution} \\
 \text{isotonic with lacrimal} \\
 \text{fluid, added to 100 cc.}
 \end{array}$$

0.125 PER CENT ZINC SULFATE SOLUTION

Calculations for isotonic alkaline buffer solution:

$$\frac{1}{82.02} \times 1.5 = 0.01829 \text{ sodium acetate factor}$$

$$\frac{0.125}{161.43} \times 1.5 = 0.00116 \text{ zinc sulfate factor}$$

$$0.04307 - (0.00116 + 0.01829) = 0.02362 \text{ differential factor}$$

$$\frac{0.02362 \times 74.55}{1.5} = 1.1739 \text{ Gm. of potassium chloride to 100 cc. of solution.}$$

5. Nicola, F.: *Gior. di farm.* 70:57, 1921.

Calculations for isotonic acid buffer solution:

$$\frac{0.5}{61.84} \times 1 = 0.00809 \text{ boric acid factor}$$

$$\frac{0.125}{161.43} \times 1.5 = 0.00116 \text{ zinc sulfate factor}$$

$$0.04307 - (0.00809 + 0.00116) = 0.03382 \text{ differential factor}$$

$$\frac{0.03382 \times 74.55}{1.5} = 1.6808 \text{ Gm. of potassium chloride to 100 cc. of solution.}$$

Formula for 0.125 per cent isotonic alkaline buffer solution:

Sodium acetate, anhydrous.....	1.0000 Gm.
Zinc sulfate, anhydrous.....	0.1250 Gm.
Potassium chloride	1.1739 Gm.

Preserved distilled water, a sufficient quantity to make.. 100.00 cc.

Formula for 0.125 per cent zinc sulfate isotonic acid buffer solution:

Boric acid, anhydrous.....	0.5000 Gm.
Zinc sulfate, anhydrous.....	0.1250 Gm.
Potassium chloride	1.6808 Gm.

Preserved distilled water, a sufficient quantity to make.... 100.00 cc.

Ten cubic centimeters of the isotonic alkaline buffer solution was titrated with the isotonic acid buffer solution, a Beckman p_H meter being used, until the final p_H of the solution was 6.75.

NOTE: It is essential in the preparation of each solution that only chemicals of the highest purity be used and that each substance be accurately weighed on an analytic balance.

0.25 PER CENT ZINC SULFATE SOLUTION

Calculations for isotonic alkaline buffer solution:

$$\frac{1}{82.02} \times 1.5 = 0.01829 \text{ sodium acetate factor}$$

$$\frac{0.25}{161.43} \times 1.5 = 0.00232 \text{ zinc sulfate factor}$$

$$0.04307 - (0.01829 + 0.00232) = 0.02246 \text{ differential factor}$$

$$\frac{0.02246 \times 74.55}{1.5} = 1.1162 \text{ Gm. of potassium chloride to 100 cc. of solution.}$$

Calculations for isotonic acid buffer solution:

$$\frac{0.5}{61.84} \times 1 = 0.00809 \text{ boric acid factor}$$

$$\frac{0.25}{161.43} \times 1.5 = 0.00232 \text{ zinc sulfate factor}$$

$$0.04307 - (0.00809 + 0.00232) = 0.03266 \text{ differential factor}$$

$$\frac{0.03266 \times 74.55}{1.5} = 1.6232 \text{ Gm. of potassium chloride to 100 cc. of solution.}$$

Formula for 0.25 per cent zinc sulfate isotonic alkaline buffer solution:

Sodium acetate, anhydrous.....	1.0000 Gm.
Zinc sulfate, anhydrous.....	0.2500 Gm.
Potassium chloride	1.1162 Gm.

Preserved distilled water, a sufficient quantity to make.... 100.00 cc.

Formula for 0.25 per cent zinc sulfate isotonic acid buffer solution:

Boric acid, anhydrous.....	0.5000 Gm.
Zinc sulfate, anhydrous.....	0.2500 Gm.
Potassium chloride	1.6232 Gm.

Preserved distilled water, a sufficient quantity to make 100.00 cc.

The directions for attaining the proper p_H , 6.75, are described under the heading "0.125 Per Cent Zinc Sulfate Solution."

SUMMARY AND COMMENT

A buffered, isotonic, preserved zinc sulfate ophthalmic solution was prepared which, by virtue of being adjusted as to reaction and tonus, was found to be nonirritating to the tissues of the eyes.

Sodium acetate was chosen as the alkaline buffer salt because it is the only one among the common alkaline buffer salts which is compatible with zinc sulfate. The use of stock sodium carbonate solution, along with an acid buffer, suggested by Gifford,⁶ produces a precipitate of basic zinc carbonate if the p_H of the acid buffer solution containing the zinc sulfate is raised to 6.75. The use of phosphate buffers must obviously be ruled out because of the very slight solubility of zinc phosphate.

By the application of buffered isotonic solutions of varying p_H to normal eyes we found that the range of comfort extends from p_H 6.5 to 7.8. Consequently, in order to place the solution well within the range of comfort and still maintain its reaction sufficiently acid to keep the zinc sulfate in solution, the preparation was adjusted to p_H 6.75.

The zinc sulfate solutions described in the preceding paragraphs, since they are devoid of irritant qualities, should add materially to the popularity and effectiveness of zinc sulfate in the therapeutic treatment of the eyes.

6. Gifford, S. R.: Reaction of Buffer Solution and of Ophthalmic Drugs: Further Note, *Arch. Ophth.* **13**:78 (Jan.) 1935.

TONOMETRIC STANDARDIZATION

A METHOD OF INCREASING THE ACCURACY OF TONOMETRY

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AND

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There are two ways whereby the intraocular pressure may be measured: manometry and tonometry. Of the two the former alone attains any degree of scientific accuracy.

Manometry, however, being a clinically inapplicable method, suitable only for the laboratory, it has been necessary to devise an instrument for estimating the intraocular pressure by interpretation of measurements taken of the impressibility of the globe. This is the method of impression tonometry.

It cannot be too strongly emphasized that the tonometer is not an instrument of accuracy in recording an absolute measure of the intraocular pressure. The tension of an eye is in part due to the pressure of its contents, but it is not identical with this pressure nor does it vary absolutely with it. Actually it is the impressibility of the eyeball which is measured by the tonometer. From this measure is deduced the tension of the eye, and the absolute pressure of the intraocular contents is inferred from this tension.

The impression tonometer, then, measures the depth of indentation produced by a given force over a constant area of the cornea. The results, however, are purely arbitrary, and in order to resolve them into absolute values the measurements obtained must be calibrated against a manometer connected directly with the intraocular contents.

The development of the tonometer and the ingenuity exercised in its design are most interesting and have been ably reviewed by Lloyd.¹ From its earliest inception there was a constant striving for more accuracy in the interpretation of the instrument's measure of ocular

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1. Lloyd, R. I.: *Am. J. Ophth.* **13**:396 and 496, 1930.

impressibility, until with the advent of the Schiötz² design a point was reached at which the actual intraocular pressure of the average eye could be inferred from the ocular tension with reasonable exactitude.

Fortunately, Schiötz was his own severest critic. The experimental manometric measurements on which he based the nomogram for use with his instrument were carried out with the most exhaustive patience and care. By his own analysis he detected errors and corrected them in their incipience, and the final measurements and calculations from which he computed his 1924 scale of pressures are models of scientific care.

Schiötz's³ experimental method was briefly as follows: He connected the eye with a water manometer and with a tonometer resting on the cornea measured the tonometer scale readings corresponding to different intraocular pressures. In each case two sets of readings were taken. First the connection between the eye and the manometer was left open. The pressure measured was the actual intraocular pressure with the tonometer in place. Second, the intraocular pressure was brought to a particular level and the connection with the manometer was then closed. The tonometer was then placed on the cornea and a reading made. Schiötz used the results of the second method to establish his nomogram, checking their accuracy by comparison with the results with the open manometer.

Schiötz⁴ recognized the fact that the values which he calculated from his experimental work were only approximations of the true intraocular pressure. He realized that while the deflections of the pointer on his tonometer were dependent on the pressure of the contents of the eye they were also dependent on a number of other factors which are variable and difficult to assess. Being unable to fit them to his formula, he assigned to them an arbitrary constant value.

The factors which determine a tonometric reading, aside from the actual intraocular pressure, are as follows:

1. The rigidity of the ocular coats.
2. The volume of corneal indentation produced by the tonometer plunger.
3. The distortion of the cornea by the tonometer foot plate irrespective of indentation by the plunger.
4. The expulsion of intraocular fluid by the weight and by the manner of application of the tonometer.
5. The mechanical accuracy of the tonometer as to: (a) adherence to specifications, (b) reduction of reading errors.

2. Schiötz, H.: *Arch. f. Augenh.* **52**:401, 1905.

3. Schiötz, H.: *Arch. f. Augenh.* **62**:317, 1909.

4. Schiötz, H.: *Acta ophth.* **2**:1, 1924; *Brit. J. Ophth.* **9**:145, 1925.

Studies on the rigidity of the eyeball and the importance of this variable in tonometry have been carefully analyzed in a brilliant contribution to the theory and practice of tonometry by Friedenwald.⁵ He grouped together and analyzed the factors involved in a tonometric reading other than pressure which he felt contributed to the resistance of the eyeball to indentation by the tonometer. He concluded:

The intraocular pressure as measured by the Schiötz tonometer with the aid of the Schiötz nomogram is subject to error due to variations in the rigidity of the ocular coats. For the same intraocular pressure the tonometer reading will be less and the pressure reading correspondingly greater, the greater the rigidity of the eyeball.

On the basis of the experimental work of Schultén,⁶ Koster,⁷ Schiötz,⁸ Ridley⁹ and Clark,¹⁰ Friedenwald derived a mathematical formula for the relation between volume and pressure changes in the eye, incorporating a numerical constant which he called the coefficient of rigidity of the eye. This formula is applicable to tonometric measurements when the pressure is taken as the actual intraocular pressure, with the tonometer resting on the cornea, and the volume is taken as the volume of the indentation produced by the tonometer plunger.

Using the original experimental data of Schiötz, he then computed the pressure within the eye at each tonometer scale reading and the corresponding volume of corneal indentation. With these calculations and his formula for the coefficient of rigidity of the eye he developed a nomogram from which may be graphically computed the coefficient of rigidity of an eye when two tonometric readings are made with two different weights. Finally, by allowing for distortion of the cornea by the tonometer foot plate irrespective of the indentation produced by the plunger, he developed a method for calculating the true intraocular pressure free from errors due to rigidity of the ocular coats.

We have made a searching analysis of Friedenwald's work and are entirely in agreement with his theory and his conclusions, all of which we have accepted *in toto* as logical and in definite order. We feel, however, that the work exhibits several drawbacks which have robbed it of some of the appreciation that should have been its due, and while we are unable to add to the fundamental concepts involved it seems highly desirable to make better use of these concepts by presenting them in somewhat less abstruse form and in such a way as to make them easily applicable to clinical tonometry.

5. Friedenwald, J. S.: *Am. J. Ophth.* **20**:985, 1937.

6. Schultén: *Arch. f. Ophth.* (pt. 3) **30**:6, 1894.

7. Koster, W.: *Arch. f. Ophth.* (pt. 2) **41**:113, 1895.

8. Schiötz, H.: *Arch. f. Augenh.* **68**:77, 1911.

9. Ridley, F.: *Brit. J. Exper. Med.* **11**:217, 1930.

10. Clark, J. H.: *Am. J. Physiol.* **101**:474, 1932.

We make no attempt within the limits of this paper to review the vast subject of tonometry, the bibliography of which is extensive. We are content with the more modest aim of using the salient points presented by various authors to evolve a clinically workable method of tonometry and one which we feel is more accurate in its interpretation of tonometric readings. In this we are following in the footsteps of Schiötz and Friedenwald, who, we believe, have done most to point out the need for tonometric standardization. Schiötz' experimental work is readily available, but it remained for Friedenwald to coordinate it in such a manner as to eliminate the important variable of the resistance to pressure which is exerted by the rigidity of the ocular envelope and thus make it possible to determine to a reasonable degree of approximation the actual resistance to tonometric pressure exerted by the intraocular pressure alone. The assumption of an average rigidity of ocular coats thus becomes inadmissible.

A study of Friedenwald's paper makes it clear that as far as theoretically possible three of the major variables in a tonometric reading have been mathematically reduced to constants, namely:

1. The rigidity of the ocular coats.
2. The volume of corneal indentation produced by the tonometer plunger.
3. The distortion of the cornea by the tonometer foot plate irrespective of the indentation by the plunger.

It is thereby possible to approximate more closely from the measured impressibility of the eye the actual intraocular pressure.

In using Friedenwald's nomogram, however, it is necessary to plot points on at least two of the pressure curves. By drawing a series of lines connecting these points with the abscissa for the zero scale reading and the curve representing the volume of fluid displaced by the weight of the tonometer one may arrive at a reading of the true intraocular pressure, without the influence of the rigidity of the ocular envelope. This procedure does not lend itself to clinical application for a number of reasons:

1. To attain any degree of accuracy would necessitate a considerable enlargement of the chart.
2. Practically, each tonometric reading would require a separate chart.
3. It is too tedious and slow a method for use in a busy clinical practice.

Our first attempt to apply the nomogram to clinical tonometry resulted in its simplification and a slight modification of its curves obtained through recalculation, especially in the region of low tension readings (fig. 1).

By application of a protractor to the modified graph it is possible to follow Friedenwald's directions and determine the slope of the line corresponding to the coefficient of rigidity for the two pressure points

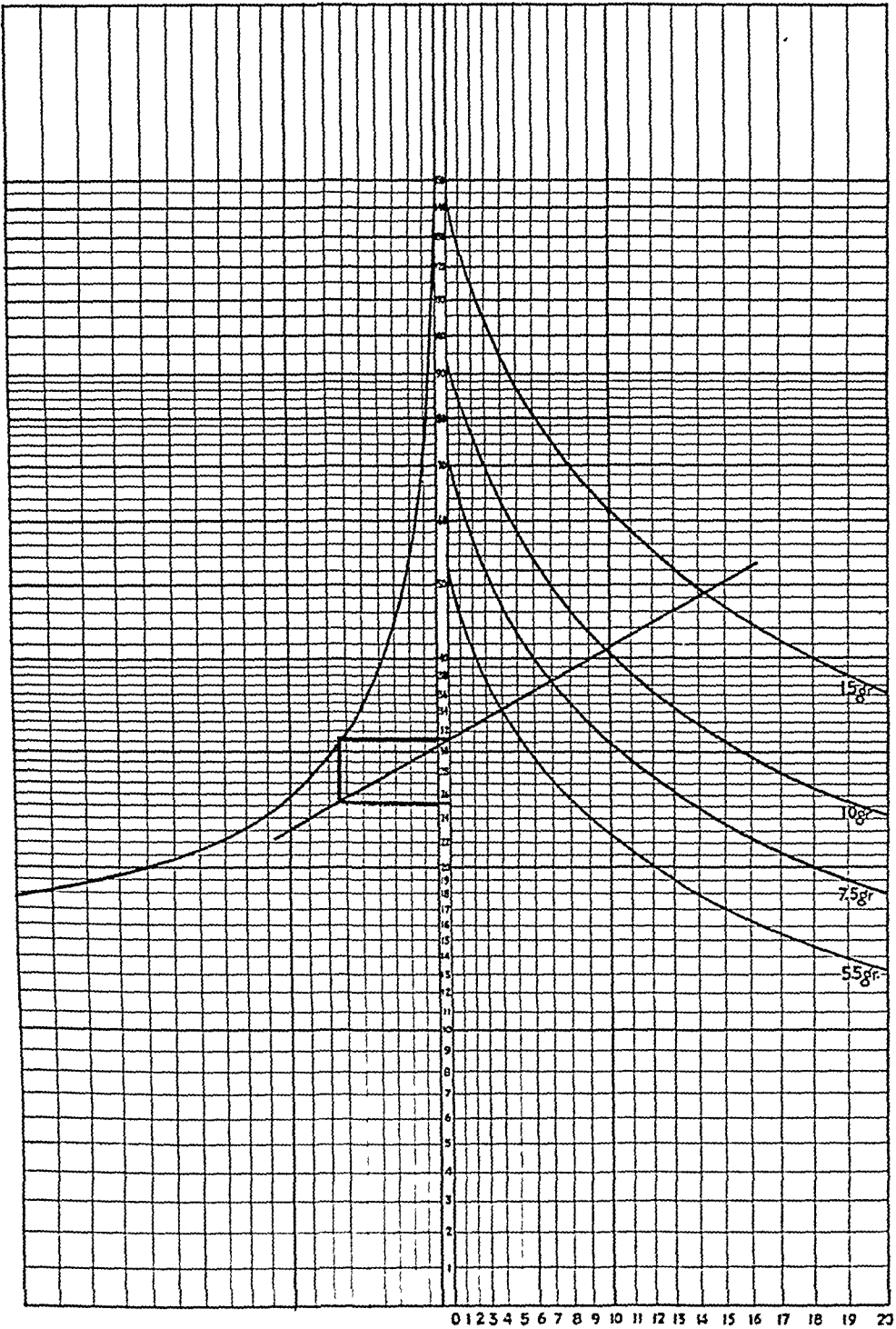


Fig. 1.—Nomogram modified from Friedenwald.

plotted. The necessary connecting lines are then drawn and the desired end point, representing the true intraocular pressure, obtained. In this procedure, however, the tediousness and the inaccuracies introduced

by the mechanical difficulties connected with plotting the graph are unaltered.

Construction of an alinement chart, which by application of a protractor would both simplify the interpretation of the readings and increase their accuracy, proved to be mathematically impossible owing to the impossibility of deriving a formula which would convert the curves of either the Schiötz or the Friedenwald nomogram into straight lines.

As a final and practical solution of the problem we have computed a numerical chart from which may be read instantly the calculated true intraocular pressure, without the influence of ocular rigidity, when two readings are taken each with a separate weight (fig. 2).

For each scale reading of the tonometer dial we have computed by means of the formulas presented by Friedenwald the actual intraocular pressure in millimeters of mercury for each of the four weights, using the 5.5 Gm. and the 10 Gm. weight for one chart and the 7.5 Gm. and the 15 Gm. weight for another. The half scale points have been interpolated. All calculations were carried to six decimal places and then rounded off. For example, if a tonometer scale reading of 4 is obtained with the 5.5 Gm. weight and with the 10 Gm. weight the dial registers 10, then by reading vertically from the 4 on the scale for the 5.5 Gm. weight and horizontally from the 10 on the scale for the 10 Gm. weight one obtains an end reading of 25 mm. of mercury as the actual intraocular pressure of the eye being tested.

Beside this figure in the same square of the chart is seen the figure 29. This represents the coefficient of rigidity of this eye in degrees of arc from the horizontal.

In Friedenwald's nomogram the slope of the line connecting the two pressure readings represents the coefficient of rigidity of the eye. This coefficient is the ratio between the logarithms of pressure at two points and the lineal measure of volume of fluid displacement in cubic millimeters. We felt, however, that the number representing this ratio would not convey the same meaning on a numerical chart as it would on a nomogram, where the slope of the line is actually pictured. Whereas the slope of a line is most truly represented by the tangent of the angle of which it is a part, the numerical value of the tangent would scarcely convey a better mental picture than the numerical value of the ratio. We have therefore represented this value on our numerical chart by the angle itself, in the belief that it is easier to visualize an angle of a given degree than a ratio representing this angle.

The slope of the line drawn through two points on two pressure curves on the nomogram that has as an end point the average normal

55	11.5	11	10.5	10	9.5	9	8.5	8	7.5	7	6.5	6	5.5	5	4.5	4	3.5	3
20	14 ⁹	17 ¹⁰	18.5 ⁵	20 ³	22 ¹	24 ⁰												
19.5	12 ¹²	15 ¹⁰	17 ⁷	19 ³	21 ³	23.5 ²	24.5 ¹											
19		13 ¹²	16 ¹⁰	18.5 ⁷	20.5 ³	22.5 ³	24 ¹											
18.5		11 ¹³	14.5 ¹²	17 ¹⁰	19 ⁷	21.5 ⁵	23.5 ³	25.5 ¹										
18			12.5 ¹⁵	15 ¹²	18 ¹⁰	20.5 ⁷	22.5 ⁵	24.5 ²	26.5 ⁰									
17.5			9 ¹⁸	13 ¹⁵	16 ¹²	19 ¹⁰	21 ⁷	23.5 ⁵	25.5 ²									
17				10.5 ¹⁹	14 ¹⁵	17.5 ¹²	20 ⁹	23 ⁶	24.5 ⁴	27 ²								
16.5				9 ²³	12.5 ¹⁵	15 ¹²	18 ¹⁰	21.5 ⁷	23.5 ⁵	26 ³	28 ⁰							
16					9 ²³	13 ¹⁹	16.5 ¹⁵	20 ¹²	22.5 ⁹	25 ⁶	27 ³	29.5 ⁰						
15.5					5 ²⁸	9.5 ²⁴	13.5 ²⁰	18 ¹⁶	20.5 ¹²	23.5 ⁹	26 ⁶	29 ³						
15						6 ²⁸	11 ²⁴	16 ²⁰	19 ¹⁶	22.5 ¹²	25.5 ⁹	28.5 ⁶	30.5 ³					
14.5							8.5 ²⁸	13 ²⁴	16.5 ²⁰	20.5 ¹⁶	24 ¹²	27.5 ⁹	30 ⁶	31.5 ³				
14								10 ²⁹	14 ²⁴	18.5 ²⁰	23 ¹⁵	27 ¹¹	29 ⁸	32 ⁵				
13.5								5 ³⁵	10 ³⁰	15.5 ²⁵	21 ²⁰	25 ¹⁵	28 ¹¹	30 ⁸	32.5 ⁵			
13									7 ³⁶	13 ³⁰	19 ²⁵	24.5 ²⁰	26.5 ¹⁵	28.5 ¹⁰	31 ⁷	34 ⁴		
12.5										8.5 ³⁶	14 ³¹	20 ²⁴	23.5 ¹⁹	27 ¹³	30 ⁹	33 ⁶		
12										4.5 ⁴²	10 ³⁷	15 ³²	20.5 ²⁶	26 ²⁰	29 ¹⁵	32.5 ¹¹	35.5 ⁸	
11.5											7 ⁴²	12 ³⁸	17.5 ³⁰	23.5 ²³	27 ¹⁸	31 ¹³	34 ⁹	37 ⁶
11												9 ⁴³	15 ³⁵	20.5 ²⁸	26 ²³	29 ¹⁷	33 ¹¹	36.5 ⁸

55	5.5	5	4.5	4	3.5	3	2.5	2	1.5	1	.5	0						
10.5	11 ⁴³	17 ³⁶	23 ³⁰	27 ²³	31.5 ¹⁶	35.5 ⁹	39.5 ²											
10	8 ⁴⁷	14 ⁴³	19.5 ³⁶	25 ²⁹	30 ²¹	35 ¹⁴	38 ⁷	41.5 ⁰										
9.5		9 ⁴⁹	16 ⁴²	22.5 ³⁴	27 ²⁸	31.5 ²⁰	36 ¹²	40 ⁵										
9		4 ⁵³	12 ⁴⁶	19.5 ⁴²	24 ³⁴	29 ²⁶	33.5 ¹⁹	39 ¹¹	43.5 ⁴									
8.5			7 ⁵⁶	15 ⁴⁹	21 ⁴¹	26.5 ³³	32 ²⁴	38 ¹⁵	42.5 ⁸									
8				10 ⁵⁸	17.5 ⁵⁰	25 ⁴⁰	31 ³¹	37 ²²	41 ¹⁴	46 ⁶								
7.5					14 ⁵⁵	21.5 ⁴⁶	28 ³⁷	34.5 ²⁸	39.5 ¹⁹	44.5 ¹¹								
7					8 ⁶¹	17.5 ⁵²	25 ⁴²	32.5 ³³	38 ²⁴	43.5 ¹⁵	49 ⁷							
6.5						11 ⁶⁴	20 ⁵³	29 ⁴³	35.5 ³⁴	41.5 ²⁵	47.5 ¹⁷							
6						5 ⁶⁸	15.5 ⁵⁹	26 ⁵⁰	33 ⁴¹	40 ³²	46 ²³	51.5 ¹⁵						
5.5							10 ⁶⁷	20 ⁵⁸	29 ⁵⁰	37.5 ⁴¹	44 ³²	50.5 ²³						
5								15 ⁶⁷	25 ⁵⁹	35 ⁵⁰	42 ⁴¹	49 ³²						
4.5								3 ⁷³	20.5 ⁶⁴	30 ⁵⁵	38.5 ⁴⁶	47 ³⁷						
4									12.5 ⁷²	25.5 ⁶³	35 ⁵⁴	45 ⁴⁵						
3.5										17.5 ⁷³	29.5 ⁶⁴	41.5 ⁵⁵						
3										9.5 ⁷⁰	24 ⁶¹	38.5 ⁵²						
2.5												27 ⁷¹						
2												5 ⁷²						

75	7	6.5	6	5.5	5	4.5	4	3.5	3	2.5	2	1.5	1	.5	0			
12	14.5 ²²	18 ¹⁷	22 ¹²	27 ⁷	32 ²	36.5 ²⁵	41 ²⁰	45 ¹⁴	49 ⁸	53 ²								
11.5		11 ²²	18 ¹⁷	23.5 ¹²	29.5 ⁷	34.5 ²	39.5 ²³	44 ¹⁸	48.5 ¹²	52 ⁶	56.5 ⁰							
11			13.5 ²¹	20.5 ¹⁷	27 ¹²	32.5 ⁷	38 ²	42.5 ²³	47 ¹⁸	51.5 ¹²	56 ⁶							
10.5				15 ²³	23 ¹⁸	29 ¹²	35.5 ⁷	40.5 ²	45.5 ²³	50.5 ¹⁸	55.5 ¹²	59.5 ⁶						
10					19 ²³	26 ¹⁸	33 ¹²	38.5 ⁷	44 ²	49.5 ²³	55 ¹⁸	59 ¹²						
9.5						15.5 ²⁹	21.5 ²³	28.5 ¹⁸	35 ¹²	42 ⁷	47.5 ²	53.5 ²³	58 ¹⁸	63 ¹²				
9							17.5 ²⁹	24.5 ²³	32 ¹⁸	40 ¹²	46 ⁷	51.5 ²	56.5 ²³	61.5 ¹⁸				
8.5								22 ²⁵	29.5 ¹⁹	37 ¹³	43 ⁷	50 ²	55 ²³	61 ¹⁸	67.5 ¹²			
8								15.5 ²⁹	25.5 ²³	34 ¹⁸	41 ¹²	48 ⁷	54 ²	60 ²³	66.5 ¹⁸			
7.5									20.5 ²⁹	29 ²³	37.5 ¹⁸	45.5 ¹²	52 ⁷	59 ²³	65.5 ¹⁸	71.5 ¹²		
7										25 ²⁹	34 ²³	43 ¹⁸	50 ¹²	57.5 ⁷	64.5 ²³	70 ¹⁸		
6.5										17 ⁶⁸	29 ⁶²	39 ⁵⁷	47 ⁴⁸	55.5 ⁴⁰	63 ³⁰	69 ²¹		
6											24 ⁶⁸	35 ⁶³	44.5 ⁵⁶	53.5 ⁴⁶	61 ³⁷	68 ²⁸		
5.5												16 ⁷²	30.5 ⁶⁶	40.5 ⁵⁹	50.5 ⁵⁰	59 ⁴⁰	67 ³⁰	
5													26 ⁷³	37 ⁶⁷	47 ⁶²	55.5 ⁵²	66 ⁴³	
4.5														12.5 ⁷⁷	29.5 ⁷¹	42 ⁶⁷	53 ⁵⁸	63.5 ⁵¹
4															21 ⁷⁷	36.5 ⁷¹	49 ⁶⁶	61 ⁶⁰
3.5																9 ⁸⁰	27.5 ⁷⁴	42.5 ⁶⁸
3																	18.5 ⁸¹	35.5 ⁷⁵
2.5																		32 ⁸²
2																		
1.5																		
1																		16 ⁸⁴

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Fig. 2.—The numerical chart from which may be read the calculated true intraocular pressure and the coefficient of rigidity in degrees of arc.

intraocular pressure of 25 mm. of mercury has an angle of $28^{\circ} 50'$, or in round figures of 29 degrees, from the horizontal. Any departure from this figure on the numerical chart presents a simple mental picture of the slope and its interpretation in terms of greater or of less ocular rigidity.

On the Friedenwald nomogram this line bears the figure 0.021, or the numerical value of the ratio mentioned.

It was Priestly Smith¹¹ who pointed out the errors introduced into a tonometric reading by a faulty position of the eye or of the tonometer during a reading. This principle is now so well known and the error so obvious as to require little comment here.

When, however, a weight is applied to the cornea the indentation and flattening produced cause an expulsion of intraocular fluid. The amount of this expulsion is dependent on the amount of weight applied and the duration of its application. The weight of the tonometer, of course, can and should be made a constant factor, but the manner and the duration of its application are variables which cannot be reduced to constants unless by the ballistics method of tonometry now being studied by Vogelsang¹² and others. It is unlikely that this factor will introduce a large error unless rather heavy weights are used for long periods. One of the objections to the single weight tonometers of McLean¹³ and Bailliant¹⁴ is the necessity of increasing their weight by a considerable amount to encompass the clinical range of intraocular pressures, thus magnifying this possible source of error. With regard to the duration of application of the tonometer, it is obvious that the longer a given weight is applied to an eye the greater will be the expulsion of intraocular fluid. Any method or instrument which will shorten this period of application by simplification of its reading will minimize this error providing the operator understands that the shortest possible time consistent with accurate observation is the goal to be attained.

In anticipation of justified criticism, it has been conceded that direct manometry is still the only scientifically accurate method of measuring the true intraocular pressure. As Schiötz and others have pointed out so emphatically, a given deflection of the tonometer needle does not indicate a definite pressure in millimeters of mercury but represents a range which is not insignificant. Nevertheless, as in all empiric work, an average point can and must be accepted if the procedure is to be at

11. Smith, O. P.: *Ophth. Rev.* **34**:65, 1915.

12. Vogelsang, K.: *Arch. f. Augenh.* **108**:714, 1934.

13. McLean, W.: *J. Ophth., Otol. & Laryng.* **20**:432, 1914; *Brit. J. Ophth.* **3**:385, 1919.

14. Bailliant, P.: *Clin. opht.* **12**:374, 1923; *Ann. d'ocul.* **160**:777, 1923.

all useful. The departure from accuracy of this middle point is dependent on the range between the maximum and the minimum determined in the experiments. The selection of a five minute angle for the test letters of the Snellen visual acuity chart is a case in point, representing as it does the average in a range of normal vision.

Schiötz also advocated the recording of intraocular pressure readings in the form of fractions, stating that "the only correct method is to note what is really seen, viz. the deflection obtained over a certain weight." He was much distressed by the tendency to record the interpreted readings in millimeters of mercury. In spite of his exhortations the clinical use of direct pressure recording has persisted and, it cannot be denied, has much to be said in its favor. This attempt at a more direct approach to the analysis of intraocular pressure has, through wide clinical use and common consent, succeeded gradually in almost replacing the original Schiötz method. It is largely responsible for the search for satisfactory direct reading instruments, such as those designed by McLean and Bailliart.

It is indirectly responsible for the confusion and lack of standardization in tonometry today.

Friedenwald's work has served to emphasize the fundamental accuracy of the findings of Schiötz. If one accepts the validity of the theory that ocular rigidity is a prime factor in the determination of actual intraocular pressure, one must automatically accept the principle of the tonometer with multiple weights and a concave plunger. Schiötz¹⁵ anticipated us in this when he convinced himself that his own X tonometer added nothing of value sufficient to warrant its adoption.

Clinical application of the increased accuracy of interpretation contributed by Friedenwald to the Schiötz method, plus the vast accumulation of clinical data based on the Schiötz scale, plus the practically international acceptance of the Schiötz nomogram, provides a widely used, clinically accurate method of impression tonometry as capable of rigid standardization and universal adoption as the Snellen visual acuity test. It remains but to devise an instrument by which this method may be fully utilized.

The Schiötz tonometer in its present form is not a standardized instrument in any sense of the word. Schiötz himself deplored the fact that reading errors with it are too great, owing, of course, to the crowded scale and the parallax inseparable from the design used in its construction.

Friedenwald stated:

The results of the clinical investigations reported indicate quite clearly that mechanical refinements in the tonometer which would reduce the error of reading

15. Schiötz, H.: *Brit. J. Ophthalm.* **11**:116, 1927.

would be of distinct value. The reading errors of the present instrument are so large that reasonably accurate estimates of ocular rigidity and intraocular pressure can be obtained only by averaging the results of repeated measurements.

We have carefully checked the weights and measurements of a large number of Schiötz tonometers, some manufactured in Europe and some in the United States. We found no instrument that adhered to Schiötz' original specifications and no two instruments that were alike in more than the diameter of the plunger.

We measured the actual downward force of the plunger with the lever and the specified weight resting on it and found wide discrepancies in the rated weights. The overhang of the long pointer was found to add an appreciable downward force when it moved from the vertical position toward the right. This additional force was consistent and would affect slightly the results obtained with the higher scale reading.

TABLE 1.—*Weights and Measurements of Schiötz Tonometers*

	Range, Gm.
Weight of tonometer (without plunger, lever or gram weights).....	10.1 to 11.45
Pressure with 5.5 Gm. weight.....	5.1 to 6.4
Pressure with 7.5 Gm. weight.....	7.05 to 9.0
Pressure with 10 Gm. weight.....	9.67 to 10.9
Pressure with 15 Gm. weight.....	14.5 to 15
	Range, Mm.
Diameter of foot plate.....	9.75 to 10.2

The increase in pressure of the plunger due to departure of the pointer from the vertical position was found to be from 3 to 5 per cent, depending on the weight of the pointer.

Somewhat the same state of affairs was noted by Friedenwald, and he pointed out that so long as the same instrument is used in each case the differences found in various readings on the same eye are of equal value for each instrument.

It would seem, therefore, either that a different nomogram should be computed for each instrument or that the instruments should be so standardized as to eliminate these variations.

The ideal tonometer must adhere rigidly to standard specifications. Each instrument must be constructed as a precision instrument, exactly like its fellow in every mechanical detail. It must be designed so as to reduce to a minimum the reading errors inherent in the Schiötz design, such as the crowded scale, the distance of the scale from the patient's eye (one of McLean's criticisms) and the parallax caused by the position of the pointer. It must incorporate an easy clinical method (such as use of our numerical chart) of converting its readings of ocular impressibility to actual intraocular pressure in millimeters of mercury without the influence of ocular rigidity. It should be so designed that it may still be used with the Schiötz nomogram as a

refined and mechanically perfect Schiötz tonometer. Finally, it should be capable within certain specific limitations of use as a direct reading tonometer.

We have attempted the design and construction of such an instrument (fig. 3).

For the minimizing of reading errors we have replaced the crowded and short arc of the Schiötz instrument by a dial divided in such a way as to magnify each scale reading by 5.

The entire dial moves, and on application of the tonometer its divisions pass before a window in the otherwise opaque front face. This window, located at the lowest point on the dial so as to decrease to a

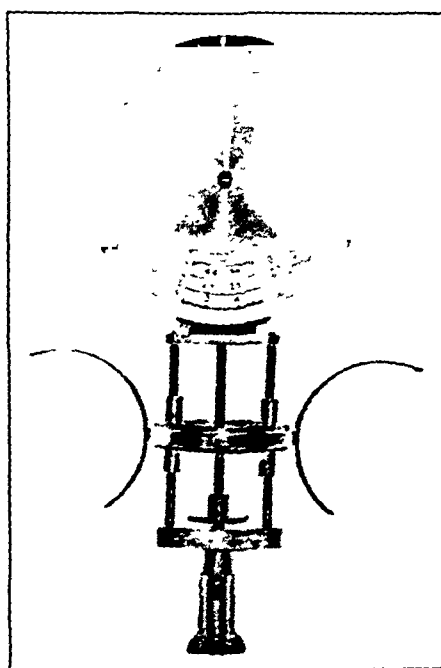


Fig. 3.—The Harrington and Parsons tonometer (patent pending).

minimum the distance the observer's eye must travel from cornea to dial, is etched on its inside surface with a fixed pointer line, thus reducing the parallax from that associated with a narrow scale and a thick pointer to virtually zero. The pivots of the various gears and levers used in motivating the dial from the plunger movement are all jeweled, as in a fine watch, so as to minimize friction.

The instrument is made largely of a very light material, so that its weight can be kept within specified limits. The foot plate and the plunger tip are made of transparent plastic to facilitate more accurate application to the cornea. Each instrument adheres rigidly to fundamental specifications, as follows:

1. The weight of the tonometer without the factors producing the downward force of the plunger, viz. the weight of the tonometer without

the weight of the plunger, the weights and the force contributed by the lever action to the plunger, equals 12 Gm.

2. The 5.5, 7.5, 10 and 15 Gm. weights are constructed so as to produce when added to the plunger a downward force equal to the specified weight.

3. The diameter of the plunger equals 3 mm.

4. The diameter of the foot plate equals 9 mm.

5. The radius of curvature of the foot plate and bottom of the plunger equals 15 mm.

Each instrument is supplied with three charts as follows:

1. A numerical chart for the 5.5 Gm. and the 10 Gm. weight and for the 7.5 Gm. and the 15 Gm. weight computed from the modified Friedenwald formula.

2. A numerical chart computed by Schiötz in 1924, with interpolation of figures for half scale readings.

3. A numerical chart corrected for an average normal rigidity of 0.021, or 29 degrees, with interpolation of figures for half scale readings.

Charts 2 and 3 are for the ophthalmologist who, not having convinced himself of the importance and the variability of the factor of ocular rigidity, wishes to use the instrument as he used his old Schiötz tonometer.

There can be no doubt as to the desirability of a direct reading tonometer. As mentioned, the search for such an instrument is largely responsible for the variety of instruments in use today and hence for the complete lack of standardization in tonometry as a procedure.

It occurred to us that, aside from using this instrument in interpreting ocular rigidity, we might use it as a direct reading tonometer providing we did not expect it to exceed its natural limitations or depart from its fundamental specifications.

In clinical practice an instrument from which the intraocular pressure may be read directly appeals greatly. Once the degree of ocular rigidity is established by a set of readings on a given eye, or the fact ascertained that the actual intraocular pressure lies well within the range of normal, all subsequent readings may with profit be read directly from the tonometer dial on the basis of an average normal rigidity represented by an angle of 29 degrees on the numerical chart.

Examination of the Schiötz nomogram (fig. 4) corrected for an average normal ocular rigidity of 29 degrees shows that with the 5.5 Gm. weight the range of intraocular pressure obtainable, this constant

rigidity being assumed, is considerable, namely from 6 to 52 mm. of mercury. With the 7.5 Gm. weight the range increases to 71 mm. of mercury. This encompasses the vast majority of clinically measured intraocular pressures, and within the region of the accepted normal range the comparison of this nomogram with the 1924 nomogram of Schiötz shows a remarkable agreement.

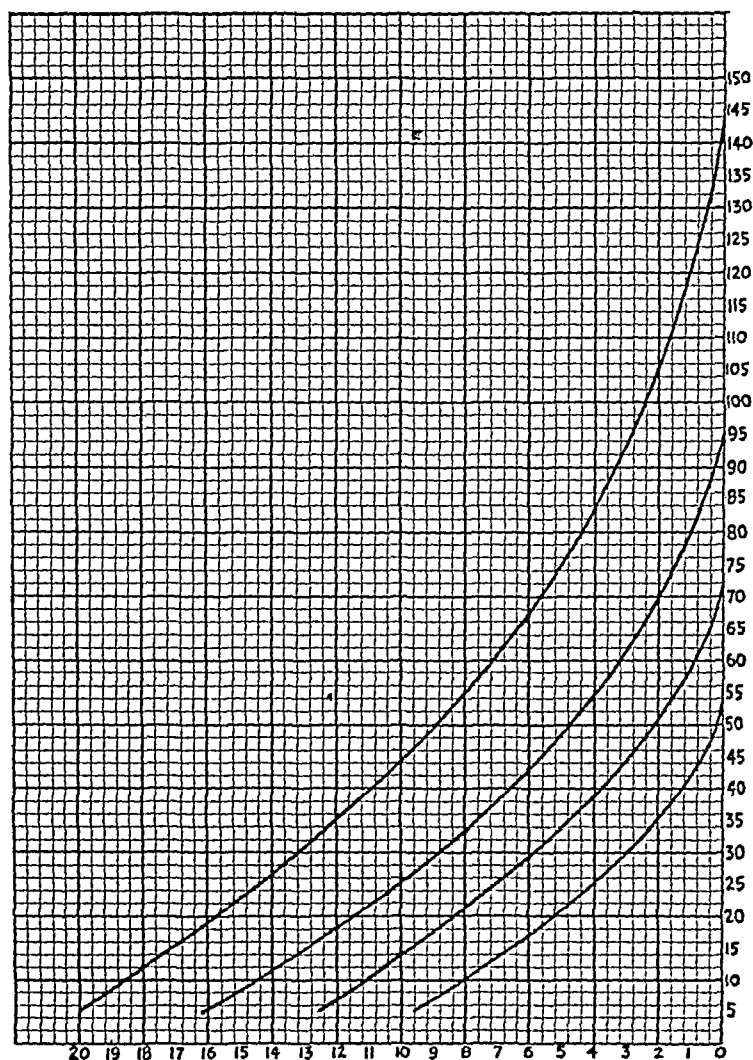


Fig. 4.—The Schiötz nomogram after 1924 experimental data corrected for an average normal ocular rigidity of 29 degrees.

There is no theoretic reason why, so long as one does not change the weights and measurements involved, one cannot transfer from the nomogram to the instrument dial the figure for intraocular pressure in millimeters of mercury for each tonometer half scale reading within this range. We have been able to do this on our tonometer, owing to the increased spacing of the tonometer scale readings, by enlarging the

window in the opaque front face of the instrument. Within the aperture of this window are two sets of figures for intraocular pressure in millimeters of mercury based on an average ocular rigidity of 29 degrees, one for the 5.5 Gm. and one for the 7.5 Gm. weight. These figures are placed directly above the regular tonometer scale and appear with the rotation of the dial with their corresponding tonometer scale reading below them. Thus we have a tonometer from which may be read directly the intraocular pressure in millimeters of mercury at the moment of its application to the cornea providing the pressure of the eye falls within the limits of the range of 6 to 52 mm. of mercury when the 5.5 Gm. weight alone is used or 7 to 71 mm. of mercury when the 7.5 Gm. weight is used and providing a single measurement is made with the assumption for the eye being examined of an average normal ocular rigidity of 0.021, or 29 degrees.

While we do not advocate this direct method of measuring the intraocular pressure, believing the ocular rigidity to be a variable rather than a constant factor, we are cognizant of its desirability as a clinical procedure. Its extreme simplicity so appeals to the practitioner that he will use a direct reading tonometer to the exclusion of other instruments even though its scale of pressures introduces confusion and its findings are inaccurate. Realizing that we cannot eliminate the use of the direct reading instrument, we believe it is expedient and in the interest of tonometric standardization to replace it by one which, though it has its ideal use as a multiple weight tonometer, is capable of direct interpretation and is more accurate than it is possible to make a single weight tonometer. Adherence of the instrument to standard specifications and the more generally accepted Schiötz scale of intraocular pressure will encourage greatly the standardization of the whole procedure.

We have purposely avoided in our discussion any mention of the relative merits of the various tonometers now in use, such as the McLean, Gradle-Schiötz,¹⁶ Bailliart and Souter¹⁷ instruments. We believe that each of these instruments in turn has contributed a great deal to the subject of tonometry, and we have no criticism of any one of them individually. The mere fact of their existence, however, is indication of the need for thorough revision of the whole subject of tonometry, and the variability of the instruments and their interpretation of ocular impressibility cries out for standardization. It is obvious that this theoretic basis for a plea for tonometric standardization must be further proved by additional work, experimental, mathematical and clinical, and we have already begun this work. For example, we have found that a

16. Gradle, H.: *Ophth. Rec.* 20:29, 1911.

17. Souter, W. N.: *Ophth. Rec.* 25:80, 1916.

difference of 0.4 mm. in the corneal radius from the average and universally accepted normal of 7.8 mm. will make a difference in volume change of the fluid displaced by the tonometer foot plate of 11 per cent. This, however, in terms of change of millimeters of mercury at normal intraocular pressure changes the reading by very little. Tables are now being computed for the various ranges in intraocular pressure.

We hope that a widespread adoption of this principle of tonometry, now made clinically available, will stimulate interest and further work and above all greater uniformity in this most important ophthalmic procedure.

SUMMARY AND CONCLUSIONS

Through the work of Friedenwald three of the variables in a tonometric reading have been theoretically reduced to constants, namely:

1. The rigidity of the ocular coats.
2. The volume of corneal indentation produced by the tonometer plunger.
3. The distortion of the cornea by the tonometer foot plate irrespective of indentation by the plunger.

The potential accuracy of impression tonometry has thus been greatly increased.

Clinical application of these fundamentally sound principles has been made practical by analysis, simplification, recalculation and the presentation of a simple numerical chart from which the true intraocular pressure without the influence of ocular rigidity may be read when two tonometer readings are taken each with a separate weight.

Representation of the ocular rigidity is included in the chart for each pair of readings.

The need for a tonometer strictly adhering to specifications is pointed out, and the desirability of tonometric standardization is stressed.

A new tonometer¹⁸ is presented, designed to minimize reading errors, adhering rigidly to fundamental specifications and capable of use as a multiple weight instrument according to the directions of Schiötz or with the new numerical chart according to the method of Friedenwald. It is also, within the natural limits of any multiple weight tonometer, a direct reading instrument.

Appended is a complete formulary, with explanations of the notations used.

18. The tonometer is manufactured by Trainer & Parsons, 228 Post Street, San Francisco.

APPENDIX

Friedenwald's table of computed values for corneal indentation and intraocular pressure with the tonometer resting on the eye (table 2) is defined and recomputed as follows:

TABLE 2.—*Computed Values for Corneal Indentation and for Intraocular Pressure with the Tonometer Resting on the Eye*

Tonometer Scale Reading	Depth, Mm.	Area of Base, Mm. ²	Radius of Base, Mm.	Volume, Mm. ³	5.5 Gm.	7.5 Gm.	10 Gm.	15 Gm.
0	0.00	7.75	1.571	0.00	52.2	71.2	94.9	142.3
1	0.05	8.75	1.669	0.41	46.1	63.1	83.4	126.2
2	0.10	9.75	1.762	0.87	41.5	56.6	75.4	113.1
3	0.15	10.75	1.850	1.38	37.6	51.3	68.4	102.6
4	0.20	11.75	1.934	1.94	34.4	46.9	62.6	93.9
5	0.25	12.75	2.015	2.54	31.7	43.2	57.6	86.4
6	0.30	13.75	2.093	3.30	29.4	40.1	53.5	80.2
7	0.35	14.75	2.170	4.02	27.4	37.3	49.8	74.6
8	0.40	15.75	2.241	4.77	25.7	35.0	46.7	70.0
9	0.45	16.75	2.310	5.57	24.1	32.9	43.9	65.8
10	0.50	17.80	2.381	6.42	22.7	31.0	41.3	61.9
11	0.55	18.92	2.455	7.34	21.4	29.0	38.9	58.0
12	0.60	20.07	2.528	8.31	20.2	27.5	36.6	55.0
13	0.65	21.25	2.601	9.34	19.0	26.0	34.6	52.0
14	0.70	22.47	2.674	10.43	18.0	24.6	32.7	49.1
15	0.75	23.71	2.748	11.58	17.1	23.3	31.0	46.6
16	0.80	25.00	2.821	12.79	16.2	22.1	29.4	44.1
17	0.85	26.31	2.894	14.07	15.4	21.0	27.9	42.0
18	0.90	27.67	2.968	15.42	14.6	19.9	26.6	39.9
19	0.95	29.05	3.042	16.84	13.9	19.0	25.3	38.0
20	1.00	30.47	3.115	18.33	13.3	18.2	24.1	36.2

COLUMN 1.—Tonometer scale readings.

COLUMN 2.—Depth of the plunger depression in millimeters, equal to $\frac{1}{20}$ of the tonometer scale reading.

COLUMN 3.—Area of the plunger depression nearest the foot plate.
Below a tonometer scale reading of 5:

$$\text{Area} = a + bD \quad \text{in which } a = 7.75 \\ b = 1 \\ D = \text{tonometer scale reading}$$

For a tonometer scale reading of 5 or above:

$$\text{Area} = (a + bd)^2 \quad \text{in which } a = 2.92 \\ b = 2.60 \\ d = \text{depth of plunger depression in millimeters} \\ \text{or} \\ \text{Area} = \pi (a + bd)^2 \quad \text{in which } a = 1.647 \\ b = 1.467 \\ d = \text{depth of plunger depression in millimeters} \\ \pi = 3.1416$$

COLUMN 4.—Radii corresponding to areas given in column 3:
 $0.56419 \sqrt{A}$ in which A represents the area

COLUMN 5.—Volume of plunger indentation of the cornea:

$$V = \frac{\pi}{3}(R^2 + Rr + r^2)h \text{ in which } V = \text{volume}$$

$$\pi = 3.1416$$

R = radius of the area of depression nearest the foot plate

r = radius of the area of depression at the base of the plunger; with a tonometer scale reading above 5, $r = 1.64$; below 5, $r = 1.571$

h = depth of depression in millimeters

COLUMNS 6, 7, 8 and 9.—Intraocular pressure with the tonometer resting on the eye, computed as follows:

Below a tonometer scale reading of 5, Schiötz' formula in Friedenwald's notation:

$$P = \frac{W}{a + bD} \text{ in which } P = \text{pressure per square millimeter}$$

W = weight used on the plunger

a = constant 7.75

b = constant 1

D = tonometer scale reading

For a tonometer scale reading of 5 or over, Friedenwald's formulas:

$$P = \frac{W}{(a + bd)^2} \text{ in which } P = \text{pressure per square millimeter}$$

W = weight used on the plunger

a = constant 2.92

b = constant 2.60

d = depth of plunger indentation in millimeters
or

$$P = \frac{W}{\pi (a + bd)^2} \text{ in which } P, W \text{ and } d \text{ are as in the preceding formula}$$

a = constant 1.647

b = constant 1.467

π = constant 3.1416

Pressures in grams per square millimeter are to be multiplied by the factor 73.5 to convert to millimeters of mercury. The constant a is a value representing the radius of the corneal indentation at the base of the plunger. The constant b is a value representing the slope of the sides of the corneal indentation.

The Fick-Maklakoff formula, $P = \frac{W}{A}$, in which P and W are as in the preceding formulas and A is the area of the corneal depression nearest the foot plate, is a completely general formula, and it will be noted that the Schiötz method and the Friedenwald method for computation of pressure differ in the determination of the value of A . The constants have been computed by Friedenwald from the Schiötz experimental data.

Divide pressures represented in centimeters of water by the factor 1.36 to convert to millimeters of mercury.

A numerical chart giving the actual intraocular pressure determined for every two tonometer readings with the 5.5 Gm. and the 10 Gm. weight and the 7.5 Gm. and the 15 Gm. weight was computed from values from which our slightly

modified Friedenwald nomogram was made. The computations were made with the following formulas:

$$P_1 = M [\log P_3 - (\log X_0 - \log X_2) \tan A]$$

$$P_0 = M [(\log Z_0 - \log Z_1) \tan A]$$

in which $\tan A = \frac{\log P_3 - \log P_2}{\log X_1 - \log X_2}$

$$\frac{P_1 - P_0}{M} = \log P_0 \text{ from which } P_0 \text{ in millimeters of mercury is obtained.}$$

Symbols:

P_3 = ordinate for greater weight.

P_2 = ordinate for lesser weight.

P_1 = ordinate for zero scale reading.

P_0 = ordinate representing actual intraocular pressure without the influence of the weight of the tonometer.

X_0 = abscissa for zero scale reading.

X_1 = abscissa for tonometer scale reading for lesser weight.

X_2 = abscissa for tonometer scale reading for greater weight.

Z_0 = abscissa for zero scale reading, identical with X_0 .

Z_1 = abscissa for scale reading for values of V_t .

M = scale modulus.

The coefficient of rigidity, R , is obtained with the formula $R = \frac{\log P_1 - \log P_0}{V_t}$, the ratio of the difference between two pressures expressed by their common logarithms and the volume change expressed in linear measure computed by means of the abscissas, representing volume change.

Friedenwald's table giving the volume of fluid displaced by the tonometer foot plate has been recomputed and extended to give this value for each pressure in millimeters of mercury at zero scale reading, as shown in table 3.

These values are arrived at as follows:

COLUMN 1.— P_t , pressure at zero scale reading in millimeters of mercury.

COLUMN 2.— P_t , in grams per square millimeter; divide P_t by 73.5, the factor for converting pressures in millimeters of mercury to grams per square millimeter.

COLUMN 3.— W_0 , the weight of the plunger that would just fail to indent the cornea; multiply P_t in grams per square millimeter by 7.75.

COLUMN 4.— W_t , the weight of the tonometer at zero scale reading; add 12 Gm. to W_0 .

COLUMN 5.— A_t , the area of support, or contact area of the foot plate, with the cornea at W_t ; divide W_0 by P_t in grams per square millimeter.

COLUMN 6.— R_t , radius of the area A_t ; multiply $(A_t)^{\frac{1}{2}}$ by 0.56419.

COLUMN 7.— $V_t = (v_1 - v_0)$ in cubic millimeters, the volume of fluid displaced by pressure of the foot plate when the resistance to the pressure of the plunger is just sufficient to give a zero scale reading.

v_1 = volume of the spherical segment formed by an average corneal radius of 7.8 mm. and a given base.

v_0 = volume of the spherical segment formed by the radius of the foot plate (15 mm.) and the same base.

TABLE 3.—*Volume of Fluid Displaced by Tonometer Foot Plate*

Pt., Mm. of Hg	Pt., Gm./Mm. ²	Wc, Gm.	Wt, Gm.	At, Mm. ²	Rt, Mm.	Vt, Mm. ³
18	0.215	1.898	13.979	57.08	4.26	19.48
19	0.259	2.003	14.003	54.17	4.15	17.34
20	0.272	2.109	14.109	51.85	4.06	15.71
21	0.286	2.214	14.214	49.75	3.98	14.38
22	0.299	2.320	14.320	47.81	3.90	13.20
23	0.313	2.425	14.425	46.10	3.82	12.18
24	0.327	2.531	14.531	44.50	3.76	11.28
25	0.340	2.636	14.636	43.03	3.70	10.53
26	0.354	2.741	14.741	41.67	3.64	9.71
27	0.367	2.847	14.847	40.42	3.59	9.09
28	0.381	2.952	14.952	39.25	3.53	8.61
29	0.395	3.058	15.058	38.16	3.49	8.11
30	0.408	3.163	15.163	37.15	3.44	7.65
31	0.422	3.269	15.269	36.20	3.39	7.24
32	0.435	3.374	15.374	35.31	3.35	6.87
33	0.449	3.480	15.480	34.48	3.31	6.53
34	0.463	3.585	15.585	33.69	3.27	6.22
35	0.476	3.690	15.690	32.95	3.24	5.93
36	0.490	3.796	15.796	32.25	3.20	5.67
37	0.503	3.901	15.901	31.59	3.17	5.42
38	0.517	4.007	16.007	30.96	3.14	5.20
39	0.531	4.112	16.112	30.37	3.11	4.99
40	0.544	4.218	16.218	29.80	3.08	4.80
41	0.558	4.323	16.323	29.26	3.05	4.62
42	0.571	4.429	16.429	28.75	3.03	4.45
43	0.585	4.534	16.534	28.26	3.00	4.29
44	0.599	4.639	16.639	27.80	2.97	4.15
45	0.612	4.745	16.745	27.35	2.95	4.00
46	0.626	4.850	16.850	26.92	2.93	3.88
47	0.639	4.956	16.956	26.52	2.91	3.74
48	0.653	5.061	17.061	26.13	2.88	3.64
49	0.667	5.167	17.167	25.75	2.86	3.53
50	0.680	5.272	17.272	25.39	2.84	3.44
52	0.707	5.483	17.483	24.71	2.80	3.24
54	0.735	5.694	17.694	24.08	2.77	3.07
56	0.762	5.905	17.905	23.50	2.74	2.92
58	0.789	6.116	18.116	22.96	2.70	2.77
60	0.816	6.327	18.327	22.45	2.67	2.66
62	0.844	6.537	18.537	21.98	2.64	2.54
64	0.871	6.748	18.748	21.53	2.62	2.43
66	0.898	6.959	18.959	21.11	2.59	2.31
68	0.925	7.170	19.170	20.72	2.57	2.25
70	0.952	7.381	19.381	20.35	2.55	2.17
72	0.980	7.592	19.592	20.00	2.52	2.09
74	1.007	7.803	19.803	19.67	2.50	2.02
76	1.034	8.014	20.014	19.36	2.48	1.95
78	1.061	8.224	20.224	19.06	2.46	1.89
80	1.088	8.435	20.435	18.78	2.44	1.83
82	1.116	8.646	20.646	18.51	2.43	1.78
84	1.143	8.857	20.857	18.25	2.41	1.73
86	1.170	9.068	21.068	18.01	2.40	1.69
88	1.197	9.279	21.279	17.77	2.38	1.64
90	1.225	9.492	21.493	17.55	2.36	1.60
95	1.293	10.017	22.017	17.03	2.33	1.50
100	1.361	10.544	22.544	16.57	2.30	1.42
105	1.429	11.071	23.071	16.15	2.27	1.34
110	1.496	11.598	23.600	15.77	2.24	1.28
115	1.565	12.126	24.126	15.42	2.22	1.22
120	1.632	12.653	24.653	15.10	2.19	1.18
125	1.701	13.180	25.180	14.81	2.17	1.13
130	1.768	13.707	25.707	14.53	2.15	1.08
135	1.837	14.235	26.235	14.28	2.13	1.05
140	1.905	14.762	26.762	14.05	2.11	1.01
145	1.973	15.289	27.289	13.83	2.09	0.98
150	2.041	15.816	27.816	13.63	2.08	0.95

V_t is found by the formula:

$$(v_1 - v_0) \text{ in which } v_1 = \pi \left[\frac{2r_1 - (4r_1^2 - d^2)^{\frac{1}{2}}}{2} \right]^2 \cdot \left[\frac{4r_1 - (4r_1^2 - d^2)^{\frac{1}{2}}}{6} \right]$$

in which $d = 2R_t$

$$r_1 = 7.8 \text{ mm.}$$

$$r_1 = 15 \text{ mm.}$$

$$\text{and } v_0 = \pi \left[\frac{2r_2 - (4r_2^2 - d^2)^{\frac{1}{2}}}{2} \right]^2 \cdot \left[\frac{4r_2 - (4r_2^2 - d^2)^{\frac{1}{2}}}{6} \right]$$

We have preferred this formula to the suggested one involving the cosine of the angle subtended by the base of the segment at the center of the sphere as it does not necessitate tedious interpolation of trigonometric values. Computations are therefore less laborious and less liable to error.

Wherever possible in these formulas and their definitions the notations of Friedenwald have been used.

In explanation of the modification of the original Friedenwald nomogram, we felt that it might be less confusing if we used the same rather than different logarithmic ratios for both ordinates and abscissas. We found it simpler to calculate our numerical chart by following this procedure and have been able to show the entire pressure range from 0 to 150 without unduly extending the nomogram.

A graphic representation may be made with any degree of expansion or contraction in either or both directions on coordinate paper whether logarithmic or otherwise, provided a consistent ratio is used in the calculations represented.

On the modified nomogram twenty divisions divided logarithmically, representing tonometer scale readings between 1 and 3 on the logarithmic scale, have exactly the same spacing as twenty divisions representing pressure readings between 1 and 3 on the logarithmic scale.

For the purpose of calculating our numerical chart we have used for the ordinates the ratio $\frac{y+10}{10}$, in which y is a pressure reading on the chart. For example, this means that for mathematical purposes a pressure reading of 10 would be equivalent to 2 on the logarithmic scale; 30 would be equivalent to 4 on the logarithmic scale, etc. The ratio $\frac{x+10}{10}$, in which x is a tonometer scale reading, is the same as for the ordinates; for example, a tonometer scale reading of 10 would be equivalent to 2 on the logarithmic scale of tonometer scale abscissas, etc. As the scale for volume change is reversed in direction, it bears the same relation to the pressure scale ordinates and tonometer scale abscissas by the ratio $\frac{30-z}{10}$, in which z is a volume change reading. For example, a volume change of 10 would be equivalent to 2 on the logarithmic scale of volume change abscissas. This method makes the chart self consistent, and the same scale modulus may be used for both ordinates and abscissas.

ABSTRACT OF DISCUSSION

DR. JONAS S. FRIEDENWALD, Baltimore: The authors' substitution of the use of a numerical table for the graphic method of calculating ocular pressure and rigidity, which I had previously proposed, has much to be said for it in respect to convenience. I should like, however, to insert one word of caution. Such a table of numbers may readily give a false sense of exactitude. If one is computing the ocular pressure and the rigidity with the aid of the graph one readily appreciates how much of an effect on the measurement an error of half a tonometric scale unit can make and thus becomes aware of the range of probable error in the measurement. A false sense of exactitude may dangerously becloud clinical judgment. Naturally, with a conscious effort the same awareness of the probable error of measurement can be achieved when one is using the numerical table, and perhaps this warning will suffice.

In attempting to set up a numerical measure of ocular rigidity I showed that a given change in the volume of an eye is always associated with a proportionate change in intraocular pressure. The proportionate change in volume varies from eye to eye, depending on the rigidity of the ocular coats. This relation can be expressed by the equation

$$\log P_2 - \log P_1 = C + R (V_2 - V_1),$$

in which P_1 , V_1 and P_2 , V_2 represent pairs of pressure and of volume measurements, while the value of R varies from eye to eye, being greater when the eye is more rigid and less when the eye is more distensible. It seems proper, therefore, to call R the coefficient of rigidity. When the logarithms are the usual ones computed to the base of 10 and the volumes are measured in cubic millimeters the value of R determined has a precise physical meaning. It is the logarithm of the proportionate change in pressure produced by 1 cu. mm. change in volume. With the nomogram which I used for graphic determination of the rigidity from tonometric readings and with the similar chart which the authors have prepared it is important to be aware of the scale on which the chart has been drawn. Since the range of pressures involved extends only slightly beyond a minimum of 10 mm. of mercury and a maximum of 100 mm., approximately 1.5 log units covers the height of the chart. The total range of volume changes covered by the charts, on the other hand, is about 50 cu. mm. If the charts had been drawn to a scale such that a horizontal distance representing 1 cu. mm. would be as great as a vertical distance representing a tenfold change in pressure the charts would have been about forty times as wide as they are tall. Such short fat charts would be neither easy to use nor printable on ordinary-shaped pieces of paper. Consequently, in drawing these charts the horizontal scale was shrunk by a factor of 25. In assigning a numerical value to a line of a particular slope on the charts, this factor of distortion in scale has of course been taken into account, so that the numbers given have genuine physical meaning.

The authors have suggested that instead of this measure of rigidity, to which a precise physical meaning can be assigned, another be taken which they define as the angle of slope of the determined line measured in degrees on the shrunk chart. The relation between the rigidity coefficient and this angle is that the rigidity coefficient is $\frac{1}{25}$ of the

tangent of the angle on the shrunken chart. This is a relation devoid of any genuine physical significance, because the factor of 25 involved has been determined arbitrarily by esthetic considerations having to do with the shape of the ordinary printed page and having nothing whatever to do with the physical status of the eye examined. I think it proper to protest vigorously against the substitution of a scale of rigidity which has no precise physical meaning for one which has such a physical meaning.

But this is not all. For further esthetic considerations the authors have chosen to plot on their chart not the logarithms of the actual intra-ocular pressures but those of these pressures enhanced by an arbitrary amount (10 mm. of mercury). At high pressures this introduces only a small change in the ratio of two pressures being compared, but at low pressures the change in the ratio resulting from this arbitrary addition may be considerable. The authors present no reason for this arbitrary change in their method of measurement. Suppose one had a tonometer which differed in diameter of the plunger from that which they have used. How would the authors propose to correlate determinations of rigidity with two such different instruments?

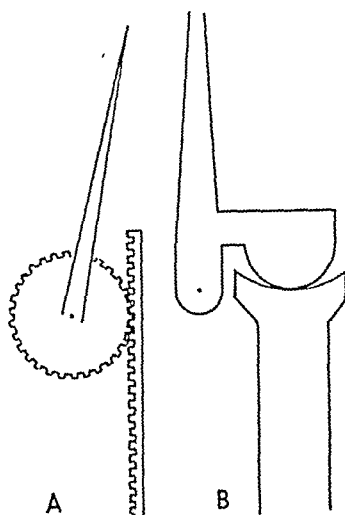
I have had the opportunity to see a photograph of Dr. Harrington's tonometer and have been much impressed with its appearance. I have not had an opportunity to study the instrument itself and should therefore prefer to reserve judgment about it. There can be no doubt, however, that the authors are decidedly on the right track. The slovenliness in construction of Schiötz type tonometers sold at a substantial price in this country is really shocking. I once weighed half a dozen instruments all produced by the same manufacturer and found variations of 2 Gm. or more in the weight of the parts which rest on the tonometer foot plate and of over 1 Gm. in the weight of the plunger and the lever arm. It would seem that the manufacturer is unaware that the mark 5.5 which he has engraved on the instrument means 5.5 Gm.

In addition to these matters of gross negligence, the construction of the Schiötz tonometer is one that tends to make the plunger stick in its collar. The average frictional resistance in brand-new instruments which I have measured amounts to about 1 Gm. The reason for this large amount of friction is simple. If one looks at the under surface of the lever arm one will find that the plunger has gouged a little pit there. I have found such pits on new tonometers freshly delivered from the manufacturer. The point of the plunger fits into this pit as it moves the lever arm up and down. Since this fixed point of contact between the plunger and the lever arm must rotate about the fulcrum of the lever arm, in some positions the tip of the plunger is deviated away from the vertical axis of the instrument. Such a tipping of the plunger interferes with its free movement in the collar which surrounds it.

Some years ago I asked Professor Morley, of the mathematics department at Johns Hopkins University, for possible solutions of the mechanical problem of converting a linear motion into a rotation, with the proviso that the moving parts must rock or roll on one another without slipping. Professor Morley produced a general solution of this problem, which I shall not attempt to expound. The two simplest examples of the application of this general solution, however, are not

without interest. The first is the arrangement of rack and pinion as shown in *A* of the accompanying illustration. This has been used in the Baillart, the McLean and other tonometers and, I believe, in the Harrington and Parsons instrument. While the rack and the pinion roll without slipping, the necessity for cogs or for pressure contact leaves a considerable source of friction. The second application of the solution is that shown in *B* of the illustration. The radius of curvature of the concave surface must be equal to the distance from the fulcrum of the lever arm to the axis of the plunger. The radius of curvature of the convex surface must be one-half this distance.

A model tonometer constructed on this plan revealed a 90 per cent decrease in friction, particularly when the surface of contact was dusted with talcum powder. In fact, the friction was so greatly reduced that the lever arm flapped widely with each pulse beat. This is undesirable in a tonometer but may afford some useful hints to any one who wishes



A, arrangement of rack and pinion. *B*, second application of general solution.

to construct an ocular plethysmograph. A damping of the rapid oscillatory movements may be achieved without increasing the friction for slow movements if a viscous oil instead of talcum powder is placed on the surface of contact. This solution of the problem of excessive friction is of course not unique. Many other equally frictionless constructions are possible.

I believe that the authors will agree with me in the assertion that standardization of the tonometer should include rigorous definitions of the permissible variations from the standard. I should like to suggest such a set of requirements for an acceptable tonometer:

1. Variations in the weight of the parts which rest on the foot plate should be less than ± 0.2 Gm.
2. Variations in the weight of the plunger with the lever arm resting on it should be less than ± 0.05 Gm.
3. Friction should be less than that overcome by 0.05 Gm.
4. Pulsations should be damped.

5. The scale should be readable to one-half the present unit.
- Further desiderata are as follows:

The scale should be close to the eye, as in the McLean tonometer. The center of gravity of the whole instrument should be low. The plunger should have the concave end and variable weight of the Schiötz model rather than the convex end of the Schiötz X model and of the McLean instrument. In addition, the instrument should be rugged and easily disassembled for cleansing, with its more delicate moving parts enclosed and protected. It should be reasonably inexpensive.

It is evident that many of these requirements are fulfilled by the instrument shown.

DR. T. L. TERRY, Boston: In reviewing the literature on tonometry one is impressed by the relative paucity of original studies and of new developments in this difficult field. The perfect solution of the problem of determining actual intraocular pressure as a clinical test lies in the development of the best substitute for manometric determination, a solution which would require in combination a physiologist, a physicist and an expert mechanic skilled in the minute accuracies of the watch maker. Harrington and Parsons are to be complimented for designing a new impression tonometer and for explaining its apparent superiority with broad consideration of the many obstacles incident to tonometry. Such work as theirs requires the utmost patience, time and skill.

It would not be difficult to raise objections and criticisms, chiefly because impression tonometry, or for that matter any form of tonometry, is through necessity not scientifically accurate, especially if the tension reading is taken directly in terms of intraocular pressure. Perhaps the foot plate is not curved in the best form; perhaps the plunger should be larger or smaller for best results. The instrument, however, will be its own best critic once it has been tested thoroughly by critical clinicians. This instrument is well worthy of such a trial before any objections are to be considered.

The plea for standardization made by the authors and by Friedenwald is most important. On a percentage basis the authors found a variation of 10 to 14 per cent in the weight, the diameter of the foot plate and the pressure obtained by use of various weights in different Schiötz tonometers. This variation should not be tolerated. It explains why the Schiötz tonometer readings taken with different instruments on the same patient are so different, and it is valid proof of the often repeated statement that one must establish the norm of one's own tonometer through tonometric readings on many patients with normal and with abnormal pressure.

Friedenwald's work to determine ocular rigidity as a means for interpretation of the intraocular pressure as shown by the tonometric reading is an important contribution, and it is pleasing to see that other experts on tonometry have confirmed his findings sufficiently to be in accord. Further observations may show that determinations of changes in ocular rigidity will lead to early recognition of the pathologic bases for the formation of scleral staphyloma, of keratoconus and of progressive myopia, since all these deformities may be preceded by specific changes in ocular rigidity or may be accompanied with such changes before the stresses of life have caused their full development. To be

more specific, however, even though the authors have stated "We have made a searching analysis of Friedenwald's work and are entirely in agreement with his theory and his conclusions," I should like to ask if they mean that they did observe the same changes in ocular rigidity with age and with ocular disease.

Although the authors included a large number of formulas in the appendix to their paper and although Friedenwald also used complicated and important formulas in his paper on tonometry, neither Friedenwald nor the present authors have given in this discussion any formula. It is now necessary for the least mathematical of the speakers to introduce a formula:

$$d = e^n$$

d represents coefficient of difficulty.

e represents embellishments and elaborations added to the simplest form of impression tonometry.

n may be 1, or unity, in simple modifications, such as the addition of a spirit level to show that the instrument is being held vertically.

n may be much greater than 1 when the embellishment would alter the design or the readings of the instrument. For instance, one may imagine an instrument with two plungers and two weights so that from two simultaneous readings the ocular rigidity could be obtained. Further, it is possible, but most probably impractical, to design a foot plate for each patient on whom tonometry is desirable so that the foot plate will exactly fit the cornea.

True, the Schiötz type of instrument is the most popular and does seem to be the most satisfactory; yet if as much time and effort were spent on study and use of the other general types, as represented by the Souter, the aplanation and the recoil tonometer, perhaps they would be found as good or better.

To me elaborations of the Souter tonometer seem important, since this instrument can be used with the patient in a sitting position, the foot plate being eliminated. It gives the least distortion of the eyeball, a point perhaps of clinical value, since rigidity, expulsion of fluid from the eye and compression of the orbital tissues behind the eye are minimal. The dangers of use of this instrument lie in the fact that there is no standard by which two observers can obtain identical results, that there are no criteria by which the amount of deformity can be determined quantitatively so that the two readings from application of different amounts of pressure can be made to determine the amount of ocular rigidity to be reckoned with and that readings made under artificial illumination are apt to be unreliable. After I had gained confidence in the use of the instrument under such illumination, a relatively disastrous diagnostic error led me to give it up in favor of the Schiötz instrument as the tonometer of choice. Although I have had no personal experience with the aplanation tonometer, surely further refinements in this type of instrument—particularly in the development of a method of accurate reading—may prove it an instrument of great clinical value, especially for determination of the coefficient of ocular rigidity and perhaps especially in instances in which the rigidity is markedly low.

The recoil tonometer if refined for routine clinical use may, on the other hand, be the instrument of choice when one wishes to obtain accurate measurements of the pressure or the rigidity of eyes of higher

pressure or of greater rigidity or both. In other words, it may be found that tonometers based on different types are to be preferred for determining the rigidity or the pressure at different levels.

It is my hope that the findings of Harrington and Parsons will be substantiated and that the ophthalmologist will find that the new tonometer is all that it appears to be—superior not only to other impression tonometers but to other types of tonometers.

May I stress again the importance of tonometric standardization. Should ophthalmologists not insist on this standardization as much as on standardization of test letters and of nomenclature?

DR. DAVID O. HARRINGTON, San Francisco: I have realized that the subject is a controversial one and have pointed out this fact. I purposely did not go into higher mathematics or derivation of formulas used in computing the numerical chart, as I felt that any one sufficiently interested would go to the appendix for this.

The slope of the angle in degrees of arc was chosen to represent numerically the ocular rigidity for two reasons: First, the slope of an angle in degrees of arc can be readily visualized by every one and furnishes ninety easily understood intervals rather than the much smaller number furnished by other suggested methods. Second, the angle itself in general contains all the factors represented in the formula for ocular rigidity, as it is the same angle that connects the abscissa for volume displacement with the values for pressure change, and in particular when the proper values are given to the base and to the perpendicular in graphic representation and trigonometric computation.

It is our impression that very few observers would pause even to consider the physical significance of any of these figures on a purely numerical chart representing nothing more than end points. The average worker judges rather by relative values only, and if relative values were maintained any purely arbitrary set of figures would serve as well as either Friedenwald's method or ours.

It is obvious, as Dr. Friedenwald has pointed out, that too much accuracy should not be attributed to any tonometer and that tonometric measurement can in no sense be compared to manometric measurement of intraocular pressure. At the same time the present state of affairs in tonometry makes it highly advisable to standardize the procedure to obtain a maximum of accuracy. The elimination of friction in the new instrument has been discussed at length in the paper. We have reduced it to a minimum by jeweling all pinions of moving parts, and whatever residual friction remained has been absorbed by the method of measuring the downward force of the plunger and its parts rather than the weights themselves. I agree with Dr. Friedenwald that a definition of specifications should be given and adhered to, and we have done this in the article.

In answer to Dr. Terry's discussion, all the measurements of the tonometer are based on the experimental findings of Schiötz. These findings were used because the Schiötz method of tonometry has had a wide clinical application for many years and the findings are based on generally accepted experimental data. Introducing a new set of figures, diameters, radii and scales would have confused the issue rather than simplified it. The whole object in presenting the paper has been to

standardize the procedure of tonometry to a system which all ophthalmologists will be able to employ with a minimum of effort, using the data most widely recognized as accurate.

With regard to the importance of ocular rigidity as a variable factor in tonometric measurements, we have felt with Dr. Friedenwald that this factor is extremely important and variable. He has investigated a large number of eyes by his method and has found clinically that ocular rigidity shows considerable variation. We have done the same with the new tonometer on a series of normal eyes of persons of different ages. I am of the impression that there is an increase in ocular rigidity which bears a relation to the age of the patient and possibly even to the changes in accommodation which occur with increasing age.

Many careful computations will have to be made before these factors have been proved.

The point introduced by Dr. Terry of attaching a spirit level to the tonometer for the better gaging of the accuracy of application is well taken. Inadvertently we have done something of this sort with our own instrument. The foot plate of the tonometer is of transparent plastic, the upper surface having the curve of a convex lens. When the tonometer is applied to the cornea one is able to see a circle of fluid beneath the foot plate, and if this circle is centrally placed it indicates accurate central and vertical application of the tonometer; in other words, it serves the same function as a spirit level.

As to the question of reading errors in the Souter tonometer, we have examined a few instruments of this type, but, have not given them serious consideration, primarily because the Souter tonometer is a single weight tonometer and, as pointed out in the paper, cannot be used, as can the Schiötz and our instrument, for demonstration of the coefficient of ocular rigidity. It is also a spring instrument, the spring introducing inevitable inaccuracy.

Ophthalmologic Reviews

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OPHTHALMIC ASPECTS OF ACUTE OXYGEN DEFICIENCY

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I. INTRODUCTION

The human eye manifests marked alterations in many of its functions when the supply of oxygen is inadequate. In fact, all the organs of the body are affected by variations in the tension of oxygen or of carbon dioxide, although certain ones appear to be more sensitive than others. The brain, for example, is more sensitive to anoxia than the smooth muscles, and the cortex appears to be more sensitive than other portions of the brain. It has been demonstrated in animals by Heymans and Bouckaert (1935) and others that cortical tissue does not recover its function if it is deprived of oxygen for more than five to eight minutes. In certain other parts of the brain and spinal cord irreversible changes do not occur for periods as long as twenty to thirty minutes. Smooth muscle can apparently go without oxygen for hours and still survive. One might therefore expect the retina to be especially sensitive to oxygen deprivation, since it is developmentally an extension of the brain and resembles it both histologically and functionally.

An analysis of the effects of anoxia on the eye might lead to a better understanding of the functions of the visual mechanism. Impaired oxidation is believed to form the basis of certain pathologic conditions of the eye. Moreover, an understanding of the effects of anoxia on vision is of clinical importance in aviation and in the understanding of certain ocular defects observed in inhabitants of high altitudes. In this paper an analysis will be made of the effects of oxygen deficiency on visual functions chiefly from the point of view of ophthalmology.

II. PHYSIOLOGIC EFFECTS OF OXYGEN DEPRIVATION

The normal atmosphere at sea level contains 20.93 per cent oxygen. There is no appreciable alteration of this percentage at even the highest

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altitude reached by man—73,000 feet (about 22,000 meters). The total atmospheric pressure, however, diminishes with increasing elevation. Therefore, the partial pressure (or absolute concentration) of oxygen decreases to a proportionate extent. Below about 30,000 to 35,000 feet (about 9,100 to 10,600 meters) the important variable concerned with physiologic changes at high altitudes is not the total atmospheric pressure but the partial pressure of oxygen. This was demonstrated by Paul Bert and later investigators, who showed that no physiologic or psychologic impairment occurs with low pressure if the subject is supplied with an adequate amount of oxygen. The essential feature of high altitudes, i. e. diminished partial pressure of oxygen, can be simulated at sea level by reducing the relative concentration (percentage) of oxygen in the inspired air. This may be done by diluting the air with nitrogen. The subject can be exposed to low oxygen mixtures in a chamber, or these may be supplied to him through a mouth piece or mask. Rebreathing devices, in which the subject consumes the oxygen of a fixed volume of air, may be used to lower the oxygen tension. By the use of low pressure chambers the atmospheric conditions encountered at high altitudes may be exactly reproduced.

Most chemical variables of the blood are rendered relatively independent of environmental changes by numerous buffer systems. Variations in temperature, for example, can be large without producing permanent damage. This is not true, however, in the case of oxygen. There is no storage unless the splenic reservoir is considered a means of storage. Even at moderate altitudes, such as those encountered in an airplane ascent, various adaptive mechanisms begin to function immediately.

The most important physiologic changes during relatively short exposures to a diminished partial pressure of oxygen are as follows: (a) stimulation of the respiratory center and an increase in pulmonary ventilation; (b) a decrease in the alveolar oxygen and the carbon dioxide tension; (c) dilatation of the alveoli, favoring a more efficient respiratory exchange; (d) an initial increase in heart rate and blood pressure and an increase in cardiac output; (e) an increase in the amount of hemoglobin in the circulation; (f) a decrease in the arterial oxygen saturation associated with the fall in alveolar oxygen tension; (g) changes in the acid-base balance, the initial effect being alkalemia associated with the excess elimination of carbon dioxide. Sudden and extreme anoxemia depresses the activity of the respiratory center so that a delayed effect may be the retention of carbon dioxide and consequently an acid reaction in the blood. The severity of the reactions to a high altitude is dependent on the following variables: (1) the height attained, (2) the rate of ascent, (3) the duration of exposure, (4) the amount of physical exertion and (5) the physiologic characteristics of the person, such as his age, physical fitness and tolerance

due to repeated ascents, and the amount of fatigue present, of sleep experienced and of alcohol consumed previous to the experiment or ascent. Authoritative discussions of the physiologic changes associated with anoxia may be found in the works of Haldane and Priestley (1935), Barcroft (1925), Loewy (1932), Peters and Van Slyke (1931) and Dill (1938).

III. PSYCHOLOGIC CHANGES ASSOCIATED WITH ANOXIA

The alterations in behavior due to oxygen want (McFarland, 1938 and 1939) follow closely the severity of the physiologic changes, indicating that sensory and mental functions depend directly on the velocity of certain chemical ones. The significant effect is due to the impairment of the oxidative processes in the nervous tissue. The psychologic changes due to anoxia are sufficiently great at 10,000 to 12,000 feet (about 3,000 to 4,000 meters) to be objectively measured by certain sensory, motor and mental tests. At moderate altitudes the impairment may be partially concealed by the exertion of greater effort. The tests which give the most satisfactory results are those in which the subject is unaware of how well or how poorly he is responding and which are relatively free from practice effects. The average person may be subjectively aware of certain physiologic changes, such as headache, alterations in breathing, motor incoordination, increased distractibility and lethargy. If the anoxia is produced suddenly and reaches an advanced stage, simulating that at altitudes of 20,000 to 25,000 feet (about 6,000 to 7,600 meters), the effects may be insidious and completely unobserved subjectively. At the more moderate altitudes of 15,000 to 18,000 feet (about 4,600 to 5,400 meters) there may be a feeling of well-being but this gradually passes, almost unnoticed, into sensory dulness and mental lethargy. In spite of obviously foolish reactions, the subject may feel confident that his mind is clear and his judgment sound, as is frequently the case in alcoholic intoxication. In the advanced stages of anoxia there is marked impairment in judgment, in memory, in emotional stability and in the functioning of the special senses. There appears to be a definite order in which the sensory and motor changes occur. Certain visual disturbances, fine tremors and motor anomalies are observed early, while hearing is maintained until the final stages of anoxia.

IV. ALTERATIONS IN VISUAL FUNCTIONS DUE TO ANOXIA

The first systematic studies of the effects of oxygen lack on certain visual functions were made by Wilmer and Berens (1918) in testing the aptitude of pilots for high altitude flying during the first World War. Standard visual tests were given to a large number of normal and of

defective subjects in the low pressure chamber as well as during exposures to oxygen deprivation with the rebreathing apparatus. The findings were reported in a series of papers in the "Air Service Medical Manual" and in medical journals (Wilmer, 1919; Berens, 1923; Sauer, 1924 and Penichet, 1922). A large part of the recent literature has appeared in foreign periodicals, and with few exceptions the work has not been carefully controlled. Only a small amount of research work has been carried out in this field in the United States. In recent years the growth of civil and military aviation has given rise to a renewed interest in the problem. The contributions reviewed briefly hereafter have brought the knowledge of the ophthalmic changes in anoxia to its present state. The findings indicate that the effects of oxygen deprivation on many visual functions provide significant data for the ophthalmologist.

As indicated previously, the retina is closely related to the brain—embryologically, morphologically and physiologically. According to Krause (1934): "The metabolism of the retina is similar to that of the brain, and not of other tissues. This is to be expected since the retina is anatomically a part of the brain. Weinstein [1932] reported that in the retina and brain the oxygen consumption and carbon dioxide production aerobically and anaerobically are similar." Nervous tissue has been shown to be particularly sensitive to a deficit of oxygen. It is consequently not surprising that investigation of certain functions that involve the retina has revealed that these also manifest extensive changes on exposure of the subject to low oxygen tension. Certain visual characteristics, such as sensitivity to light, are affected more easily than others, such as visual acuity or size of the visual fields. It has not been possible to determine to what extent the effects of anoxia on vision are due to alterations in the central nervous system and to what degree the sense organ itself is affected. There is an increasing amount of evidence from data such as those reviewed here, however, which seems to indicate that the neural components of the retina and of the brain are more extensively involved than was originally supposed, even in such characteristics as sensitivity to light and visual acuity.

1. *Visual Sensitivity: Light Sense and Dark Adaptation.*—One of the most direct and fundamental tests of visual functioning consists in measurement of sensitivity to light, i. e. the light threshold, or the intensity of light which is just sufficient to be perceived subjectively. The determination of the light threshold over a stated time interval in the dark indicates the occurrence of a gradual increase in sensitivity traditionally classified as dark adaptation.

Pilots have frequently reported a general darkening of the visual field while flying at great heights without oxygen (18,000 feet, or about

5,400 meters, and above). In Douglas bag or rebreathing experiments in the laboratory various observers have noticed a dimming of the lights during sudden exposure to partial pressures of oxygen simulating those at altitudes of from 12,000 to 14,000 feet (about 3,600 to 4,200 meters) and a marked increase in the brightness of lights on being quickly changed back to room air. A number of studies have been made of this phenomenon with rather crude experimental technics. More recently it has been subjected to precise measurement with a special adaptation of the biophotometer and with the Hecht adaptometer, the usual procedures being employed. In relatively crude experiments with an optical wedge, Wilmer and Berens (1918) found that during the rebreathing test the light sensitivity showed an improvement in 25.9 per cent of their subjects, no change in 44.5 per cent and a decline in 29.6 per cent. With a similar apparatus used during trans-Pacific flights at 11,000 to 12,000 feet (about 3,300 to 3,600 meters) McFarland and Edwards (1937) observed a decrease in light sensitivity in most of the subjects.

Dark adaptation under conditions of oxygen deprivation has been fairly extensively studied abroad. Tanaka and Sekiguchi (1935) exposed 12 normal subjects to low pressure and tested their sensitivity with a Nagel adaptometer. They reported a decrease in dark adaptability which was proportional to altitude and which could be counteracted by administration of oxygen. They found that during prolonged exposure to a pressure corresponding to that at 3,000 meters (about 10,000 feet) the sensitivity tended to return toward normal. At 4,000 meters (about 13,000 feet), on the other hand, continued exposure resulted in further deterioration.

Fischer and Jongbloed (1935) studied the dark adaptation of 2 subjects in a low pressure chamber. They measured the time in darkness after exposure to a bright light which elapsed before a lamp of standard intensity could be perceived through various filters. They did not obtain either the final threshold or the recovery curve. On the basis of their criteria they reported a slight "delay" of dark adaptation at 3,000 meters (about 10,000 feet) and a marked "delay" at 6,000 meters (about 20,000 feet). They interpreted this change as ". . . the physiological expression of interference with the regeneration of the photosensitive substance of the retina." Further studies have shown that this interpretation is probably erroneous. Bunge (1936) administered low oxygen mixtures (8 to 11 per cent of oxygen) to 7 subjects by means of an artificial respiration apparatus and measured their dark adaptation with the Engelking-Hartung instrument. He found that after complete dark adaptation in normal air, exposure to a low oxygen mixture resulted in a decrease of retinal sensitivity. Since this change took place in a dark-adapted subject, destruction of visual pigments, or a delay in their regen-

eration, could hardly have been involved. Moreover, administration of oxygen resulted in a return of retinal sensitivity at a rate which was more rapid than could be accounted for by regeneration of the visual purple. Vishnevskiy and Tsyrlin (1935, 1936) found that a lowered atmospheric pressure produced a decrease not only in the light sensitivity but in the electrical excitability of the eye. They concluded that since the latter does not involve the photochemical system anoxia has its effect primarily on the neural tissue of the visual mechanism. Clamann (1938) expressed the belief that an extraretinal process is involved because in his studies on 3 subjects monocular thresholds were affected differently from binocular thresholds.

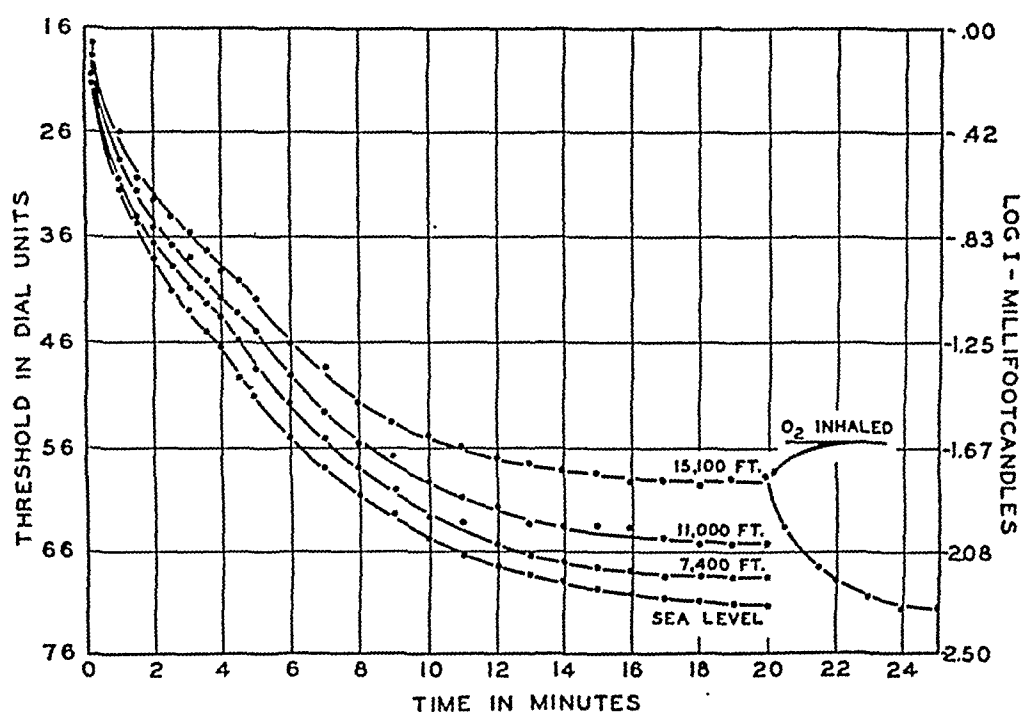


Fig. 1.—Alterations in dark adaptation under reduced oxygen tensions. Composite curves representing data for 20 subjects are presented. Intensity thresholds (minimum visible light intensities) are plotted in relation to time after exposure to a bright light. The higher the threshold the less is the sensitivity of the visual mechanism. As the oxygen tension is diminished the entire curve is displaced upward along the intensity axis of the graph, indicating impaired sensitivity. After enough time had elapsed at 15,100 feet (about 4,600 meters) so that no further change in sensitivity took place, oxygen was administered. The light sense then returned to normal in about three minutes. (From McFarland and Evans, 1939.)

An extensive study of light sensitivity was made by McFarland and Evans (1939) with a biophotometer specially adapted so that precise measurements could be obtained for experimental purposes. Twenty subjects were tested at altitudes varying from 7,400 to 15,100 feet (about 2,200 to 4,600 meters) simulated in a low oxygen chamber. Figure 1

shows the composite dark adaptation curve at each altitude as well as the effects of giving oxygen at the end of the experiment. The thresholds are plotted against time in darkness. Elevation of the curve signifies decreased sensitivity. Even at 7,400 feet the mean threshold rise was 0.1 logarithmic unit. At this altitude, therefore, the test light had to be made about one and one-fourth times brighter than under normal conditions in order to be seen by the subject. At 15,000 feet (about 4,500 meters) the thresholds rose an average of 0.4 logarithmic unit. In other words, a light intensity two and one-half times normal was required in order to be seen. The shape of the curves is apparently not altered; hence the rate of adaptation is not affected. When oxygen was given, complete restoration of retinal sensitivity took place in a few minutes. McDonald and Adler (1939) found changes of a similar order of magnitude with the Hecht adaptometer. They observed that anoxia causes an equal elevation of the rod and of the cone threshold, whereas vitamin A deficiency produces a greater change in the rod threshold. They suggested this as evidence that different mechanisms are involved in the two cases.

In experiments with the Hecht adaptometer, McFarland and Forbes (1940) found that oxygen deprivation and hypoglycemia have similar and additive effects on dark adaptation. Moreover, administration of an excess of either oxygen or dextrose serves to diminish greatly or to compensate for a deficiency of the other substance. It is well recognized that the brain is less able to burn fats and proteins than other parts of the body, and dextrose appears to be the main metabolic substrate. A reduction in blood sugar, therefore, would be expected to reduce the oxidation in the brain and if sufficiently advanced could impair sensory and mental functions in the same way as anoxia. In both cases there is a reduction in oxygen in the nerve tissue; so oxidation should be increased by giving dextrose in the case of anoxia and oxygen in the case of hypoglycemia. This hypothesis was tested by using thresholds of light sensitivity as criteria for decreased or increased sensitivity. The blood sugar was lowered by injecting insulin, and then the oxygen tension was increased. On other occasions the authors exposed subjects to low oxygen tension and then increased the blood sugar. Figure 2 shows that when the blood sugar was lowered by insulin the thresholds increased; then the subjects inhaled oxygen from a cylinder, and the thresholds returned to normal; when the subjects were returned to room air the thresholds again rose, and, finally, when the subjects ingested dextrose normal sensitivity returned. In other experiments the combined effects of anoxia and hypoglycemia produced striking impairment. It is suggested that a deficiency of either substance (dextrose or oxygen) interferes with oxidative processes which are essential to neural functioning and consequently to vision.

The results relating to the effect of variations in blood sugar content on visual function have significant implications in the fields of psychology, ophthalmology and aviation. If a variation in the blood sugar content of 20 to 40 mg. per hundred cubic centimeters of blood (the usual difference between the basal and the nonbasal state) can double the intensity threshold, it would appear that such variables should be controlled in experiments. It is possible that certain ocular defects might be more clearly understood if the effects of variations in the blood sugar content were studied. In aviation the application is more direct, for pilots might benefit from the ingestion of dextrose in flights at high altitudes.

McFarland and Forbes (1940) also confirmed and extended the previously reported observations on anoxia and dark adaptation. The dark adaptation curves were first determined with the low oxygen chamber at sea level and then at various simulated altitudes. Both the

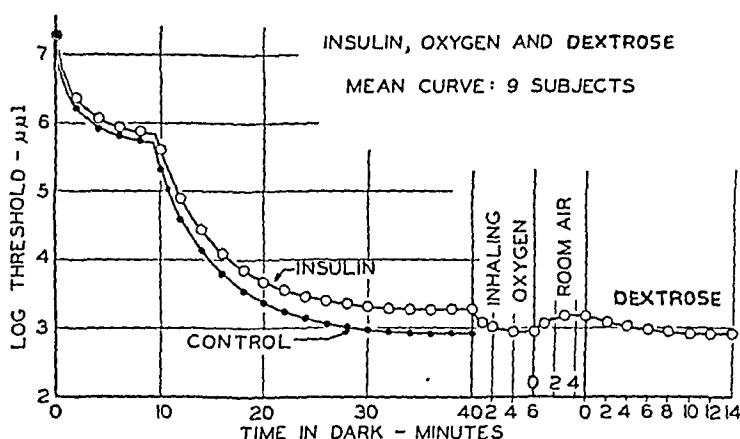


Fig. 2.—The effects of insulin, oxygen and dextrose on light sensitivity. When the blood sugar level is lowered by the injection of insulin (5 to 8 units) the dark adaptation curve becomes elevated as compared with that of the control. This resembles the effect produced by anoxia, shown in figure 1. A further relation between anoxemia and hypoglycemia is demonstrated by the fact that inhaling pure oxygen counteracts the effects of insulin; subsequent withdrawal of the pure oxygen again reveals the lowering in sensitivity due to insulin. Finally, the administration of dextrose restores normal light sense. It has also been shown that hyperglycemia produced by ingestion of dextrose can partially counteract the effects of anoxemia on light sensitivity. (From McFarland and Forbes, 1940.)

rod and the cone portions of the curves were elevated progressively with increasing anoxia. At 20,000 feet (about 6,000 meters) the effects were marked, the final rod threshold in 1 case being raised by a factor of 4. These changes were immediately abolished on administration of oxygen. The authors attributed the effects to the neural elements of the retina and of the central nervous system rather than to the regeneration of the photochemical substances of the retina, since the threshold continued to rise with increasing oxygen lack even in the completely dark-adapted

eye. Furthermore, the recovery of light sensitivity was much more rapid with oxygen than with any known chemical substance, such as vitamin A, and the restoration was comparable in time and extent to that observed in other cortical functions, such as memory or complex reactions. These findings indicate a broader basis for visual functions. Not only does dark adaptation appear to be related to photochemical processes in the retina, but oxidation in the nerve tissue plays an important role.

2. *Differential Sensitivity*.—Schubert (1932) and Gellhorn (1936 a) have observed a considerable decrease in visual intensity discrimination while inhaling 8 to 10 per cent oxygen. They used Masson disks, with which this function can be crudely measured. When these disks are rotated a series of rings of different shades of gray are seen. The number of rings that can be seen is a measure of the ability of the eye to discriminate differences in intensity. Gellhorn (1936 b) found also that the effect on the visual intensity discrimination of breathing 8 to 9 per cent oxygen can be either completely removed or greatly diminished by a small concentration of carbon dioxide (3 per cent). This percentage of carbon dioxide in the absence of anoxia had no effect on the sensory function investigated. These authors stated the belief that this effect was due to circulatory improvement.

3. *Visual Acuity*.—Since a high degree of visual acuity is considered a prerequisite in an airplane pilot it is important to know how this characteristic is affected by anoxia. Earlier investigations were not conclusive. Wilmer and Berens (1918) made tests with the Ives object in the low pressure chamber and with a rebreathing device. They found no change in 60 per cent of their 25 subjects, an improvement in 12 per cent and a decrease of visual acuity—the amount of which was not stated—in 28 per cent. On the other hand, Bagby (1921), also using a Henderson rebreather and the Ives test object, found no significant change in visual acuity until just before the subject collapsed, when there was a marked deterioration not only in the sensory function but in the capacity to attend and in the ability to cooperate.

More recently Berger and Bøje (1937) tested the ability of 2 emmetropic subjects to resolve two squares while breathing air containing 8.7 per cent oxygen, air corresponding to that at 22,500 feet (about 6,900 meters). Two stimulus patterns were used: luminous squares on a dark field and black squares on a white field. As the squares were moved apart the authors measured the minimum distance between them at which they could be recognized as separate; also, as they were approximated the point at which they seemed to fuse was recorded. They reported that in spite of marked oxygen lack the resolving power was unchanged or only slightly decreased while luminous squares were

used. With black squares on a white background, on the other hand, a considerable decrease was found; the thresholds rose 30 per cent in 1 subject and 100 per cent in the other. They attributed this change largely to an alteration in the intensity discrimination threshold. It is interesting to note that a similar condition was found in the case of the peripheral field; this seemed to shrink for black objects on a white field and to remain unaltered for white objects on a dark background. Furuya (1937) reported a decrease in visual acuity at altitudes above 20,000 feet (about 6,000 meters).

Visual acuity is dependent among other things on the intensity of illumination. In order to discuss the behavior of visual acuity during oxygen deprivation it is necessary to review this relation. It was not considered in the investigations mentioned and probably accounts for the inconsistencies in the findings.

Uhthoff (1886, 1890) made the first thorough investigation of the relation between visual acuity and illumination over a great range of intensities using white and colored lights. A few years later Koenig (1897) made such comprehensive observations that his data have become classic. The most adequate and precise measurements were described recently by Shlaer (1937), who plotted the logarithm of visual acuity (vertically) against the logarithm of intensity of retinal illumination (horizontally). For white light a distinct break appeared in the curve. The portion of the curve below the point of discontinuity is believed to represent rod vision; the upper portion, representing measurements in brighter light, is believed to describe cone vision. The data of Koenig for white light are similar when plotted in this manner (Hecht, 1937). If red light (to which the rods are believed to be relatively insensitive) is used instead, with central fixation, the rod portion of the curve is deleted and the data fall on a single continuous curve. This is believed to represent only cone vision. Shlaer, Smith and Chase (to be published) showed that this curve corresponds to a theoretic equation derived by Hecht (1934) on the basis of the simplest assumptions concerning the kinetics of a photochemical receptor system.

The relation between foveal visual acuity and illumination under reduced oxygen tension was studied by McFarland and Halperin (1940) in 11 subjects. Various mixtures of nitrogen and oxygen were inhaled from a mask. The visual acuity apparatus described by Shlaer was used. The intensity of illumination could be set in steps of about 0.3 logarithmic unit (i. e., at each step the intensity is approximately doubled). The test object consisted of the projected image of a Landolt broken circle, or C. The size of this object could be varied continuously over a range of about 1:100 at a fixed distance of 1 meter from the eye. Red light was used.

The results of this study can best be described by reference to figure 3, which presents the data for 1 subject. The curve at the left shows the relation between foveal visual acuity and illumination in normal air. With increasing illumination the visual acuity rises rapidly at first and then at a gradually decreasing rate until a maximum is reached and the curve becomes horizontal. The curve at the right, passing through the solid circles, represents the tests at a simulated altitude of 18,000 feet (about 5,400 meters). The curve has shifted horizontally to the right along the intensity axis. As a consequence of the shape of the curve such a shift results in a relatively large decrease of visual acuity at low illuminations. At increasing light intensities anoxia produces less and less change. At very high illuminations the decrease is negligible. This may account for the inconclusiveness of the earlier experiments.

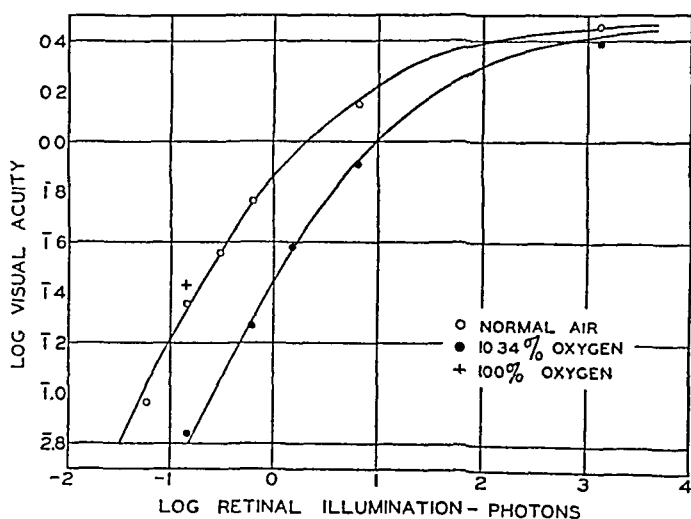


Fig. 3.—The effects of anoxia on foveal visual acuity. Visual acuity is plotted vertically and intensity of illumination horizontally.¹ The curve at the left shows how visual acuity varies with light intensity in normal air. When the subject was exposed to a low oxygen mixture equivalent to that at 18,000 feet (about 5,400 meters) the entire curve was displaced to the right along the intensity axis. Consequently, vision in dim light is markedly impaired, whereas in intense illumination (where the vertical distance between the curves is very small) the change in visual acuity is negligible. The plus sign represents a final control measurement with pure oxygen after the measurements during anoxia had been completed. (From McFarland and Halperin, 1940.)

The magnitude of the drop in foveal visual acuity at low illuminations on exposure to anoxia is large. For example, with an intensity of 0.144 photon¹ ($\log 1 = 1.159$) the visual acuity decreased at 10,000 feet

1. Definitions of units employed: Visual acuity is expressed as the reciprocal of the angle, in minutes, subtended by the finest detail distinguishable, which here

(Footnote continued on next page)

(about 3,000 meters) to 68 per cent of normal and at 18,000 feet (about 5,400 meters) to 45 per cent. When, on the other hand, the illumination was high, anoxia produced only a negligible change in visual acuity. Thus, with 1,320 photons ($\log 1 = 3.120$) the visual acuity remained at 94 per cent of normal even at 18,000 feet. As a practical application of these findings it may be concluded that—so far as foveal visual acuity is concerned—it is much more important that airplane pilots be provided with oxygen during night flights than during daylight flights.

It has been shown that both for dark adaptation and for visual acuity there is a shift of the curves upward along the intensity axis. This shift is of about the same order of magnitude for the two. One might think of the effect of anoxia as being equivalent to that of putting an optical filter before the subject's eyes. Indeed, one notices subjectively a general darkening of the visual field during anoxia. When oxygen is then administered there seems to be a marked brightening of the field.

4. *Visual Fields, Peripheral and Central.*—The effects of anoxia on the extent of the peripheral visual field have been studied by a few investigators. Wilmer and Berens (1918) made the first measurements, in a low pressure chamber. They found that there was usually a slight enlargement of the field for form and for color at simulated altitudes of 5,000 feet (about 1,500 meters) and 10,000 feet (about 3,000 meters). This was followed by a contraction which was slight at 15,000 feet (about 4,500 meters) and became marked at 20,000 feet (about 6,000 meters). The shrinkage was greatest inferiorly, where (for white) the field averaged 14 per cent of normal, or about 7.7 degrees. A lesser change was demonstrable in the other prime meridians. The method of perimetry employed was not described.

Without being aware of these studies, Goldmann and Schubert (1933) made similar investigations, in a low pressure chamber as well as with low oxygen mixtures. They made their tests with a square black object on a white field. They found chiefly a shrinkage of the nasal and superior portions of the field. This contraction amounted to over 25 degrees in one of the authors and up to 15 degrees in other subjects at 6,500 to 7,000 meters (about 21,500 to 23,000 feet). Temporally the contraction was not demonstrable or was slight. The alterations began at about 14,000 feet (4,200 meters) and were counteracted by breathing oxygen. The authors stated the belief that the contraction of the nasal portion could be caused only by an alteration in the retina itself, since depression of the central nervous system would result in concentric or

corresponds to the gap in the C used as the test object. Retinal brightness is given in photons (Troland, 1916) and is expressed as external brightness in millilamberts times $10/\pi$ times pupil area in square millimeters (photons = millilamberts $\times 10/\pi \times$ pupil area in square millimeters).

homonymous contraction of the field. They explained the asymmetry of ~~contraction as being due to an inequality of the blood supply to different~~ parts of the retina.

Furuya (1937) reported low pressure chamber experiments on 6 subjects. He described a contraction of the field which began at about 5,000 meters (16,400 feet). At first this was noted temporally, especially above. Continued exposure at the same altitude resulted in accentuation of the effect, which was more marked in sympathicotonic than in vagotonic subjects.

Similar experiments were carried out by Kyrieleis, Kyrieleis and Siegert (1935) with a technic somewhat different from that employed by Goldmann and Schubert. They used white objects on a dark gray background. They found that although the altitudes simulated were as high as 8,000 meters (26,000 feet) there was no demonstrable contraction of the visual field which exceeded the unavoidable error of 1 to 3 degrees. On the contrary, there frequently appeared a concentric widening of the field at the onset of anoxia. One of their subjects had served for Goldmann and Schubert's experiment, in which considerable contraction had been noted. Kyrieleis and his co-workers attributed the difference largely to the method used. They expressed the opinion that the use of white stimuli on a dark field gives results which are less likely to be affected by "weakening of attentiveness" than those obtained with black stimuli on a bright field. Elsewhere Kyrieleis described a physiologic weakness of attention in the nasal portion of the field. In view of the inconclusiveness of the effects of anoxia on visual acuity before the role of illumination was considered, it seems reasonable to expect that investigations of the peripheral visual field in various intensities of illumination might also resolve some of the existing discrepancies.

The behavior of the central visual field during oxygen lack have been studied by Evans and McFarland (1938). Experiments in a low oxygen chamber revealed a progressive widening of the angioscotoma (projected defect related to the retinal perivascular spaces). This began at a simulated altitude of about 13,000 feet (about 4,000 meters), and became more marked with increasing "elevation" until the visual field was obliterated except for an area 8 to 10 degrees about the macula (fig. 4). Administration of oxygen resulted in a complete return to normal. The measurements were made on a stereocampimeter with white test objects 0.4 mm. in diameter 190 mm. from the eye. The background was dull black paper under an illumination of 15 foot candles. Goldmann and Schubert (1933), using 5 mm. white and colored objects, found an enlargement of the blindspot. Conversely, it was reported by Rosenthal (1939) that on administration of 100 per cent oxygen to normal persons the width of the angioscotoma was diminished.

Seitz and Rosenthal (to be published), using the procedure of measuring the changes in the angioscotoma described by Evans (1938), found that the local administration of strychnine at sea level caused a marked narrowing of the scotoma in the treated eye. No such change was apparent in the untreated eye, which suggests that the effect was on the retina itself rather than on the more central tissue. Then they administered strychnine while the subjects were exposed to an oxygen lack simulating that at 17,500 feet (about 5,300 meters). The drug appeared to counteract the widening of the scotoma resulting from the anoxia. This is consistent with the concept that oxygen lack depresses the activity of the neural elements of the retina.

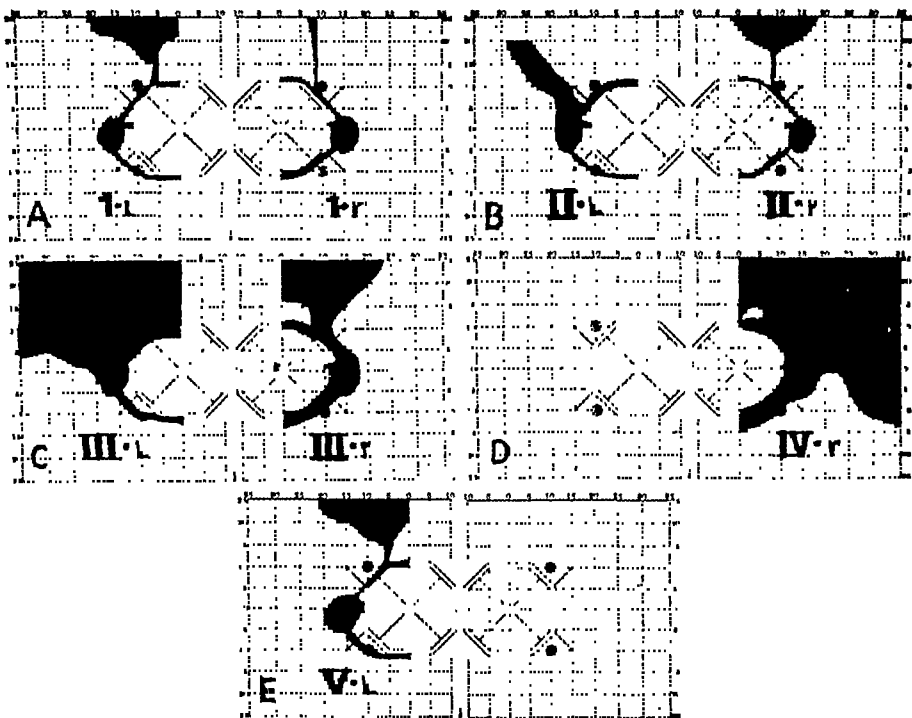


Fig. 4.—The effects of oxygen deprivation on the central visual field. *A*, sea level, 20.96 per cent oxygen; *B*, 13,000 feet (about 3,900 meters), 12.60 per cent oxygen; *C*, 17,000 feet (about 5,100 meters), 10.64 per cent oxygen; *D*, 22,400 feet (about 6,800 meters), 8.69 per cent oxygen; *E*, sea level, 20.96 per cent oxygen. The usual method of angioscotometry was employed, with a minute object. The black areas are the projections of the functionally depressed portion of the retina. These correspond to the inferior part of the retina. As the oxygen supply is progressively decreased the scotoma widens until the visual field for the stimulus object is completely obliterated except for a region 8 to 10 degrees about the macula. The return to normal was complete five minutes after inhalation of oxygen. (From Evans and McFarland, 1938.)

In Evans' original studies of angioscotometry it was suggested that the variations in the size of the scotoma might be indirectly attributable to the increase in the size of the retinal vessels. More recently, however,

Evans has stated that other factors are more basic, such as the impairment of the synapses in the retina. In the study by Evans and McFarland (1938) of the effects of oxygen lack on the angioscotoma frequent observations were made of the eyegrounds with an ophthalmoscope. Since only minor changes were observed in the size of the retinal vessels, this factor was considered to be of minor importance in causing the marked variations in the size of the scotoma. During the height of the anoxia the color of the artery and that of the vein approached one another, but at no time was it difficult to distinguish one from the other. When oxygen was administered at the end of the experiment the artery assumed its characteristic color. There was no evidence of marked vasodilatation or constriction, nor was there evidence of arterial alteration, edema or hemorrhage. It is possible that edema and other changes would have been ophthalmologically visible had the subjects remained in the low oxygen chamber for longer periods.

Recently Cusick, Benson and Boothby (1940) studied the effects of anoxia and of high concentrations of oxygen on the retinal vessels. A brief report of their experiment follows:

Two different methods of measurement were used: the Morgan graticule and a prism displacement method developed by Dr. C. W. Rucker . . . A number of observations were made in the low pressure chamber at pressures simulating altitudes of 18,000 to 21,000 feet [about 5,400 to 6,400 meters]. In other cases anoxia was produced by a nitrogen-oxygen mixture. With anoxia there was measurable increase in the size of the vessels, varying between 10 and 20 per cent, which was more marked in the veins. Following this, another group of subjects was given essentially 100 per cent oxygen by means of the B. L. B. inhalation apparatus [Boothby and Lovelace, 1938] with the rate of flow at 9 liters per minute continued for thirty minutes. In this group there was a measurable decrease in the size of the vessels [10.5 to 37.7 per cent for arterioles and 16.2 to 37.5 per cent for veins, with an average of 24 and 28.2 per cent, respectively].

The authors concluded that the ". . . changes in the size of angioscotomata in the visual field in these two conditions may be, in part at least, due to changes in the caliber of the retinal vessels."

5. *Color Vision*.—Investigations of color vision with the more common clinical means, such as Stilling's plates, have revealed no changes at high altitudes (Wilmer and Berens, 1918). Vishnevskiy and Tsyrlin (1935, 1936) measured retinal sensitivity to red, green and blue light with the Nagel adaptometer and appropriate colored filters. They reported that low pressure resulted in a greater decrease of retinal sensitivity to these colors than to white light. The colored lights seemed to be less saturated; in fact, green and blue often appeared colorless at threshold intensity. Inhalation of oxygen for periods up to twenty-five minutes did not completely restore the sensitivity to color, although the sensitivity to white light and to electrical stimulation recovered com-

pletely. The authors concluded that cone vision is affected to a greater extent than rod vision. It is difficult to evaluate their findings, since their technic is not completely defined. Their apparatus was crude in comparison with the Hecht-Shlaer adaptometer (1938), for example. Dark adaptation curves obtained by use of the latter show a discontinuity at the point where cone function is superseded by rod function; alterations in the two can thus be separately evaluated. When colored lights are used they appear colored at threshold intensities corresponding to the cone portions of the curve and colorless thereafter even in normal air. With red light of a wavelength to which the rods are relatively insensitive, only the cone portion of the curve is obtained with central fixation; hence, it is not surprising that this did not lose its color in Vishnevskiy and Tsyrlin's study, whereas green and blue did. By use of the Hecht-Shlaer apparatus, McDonald and Adler (1939) found that rod vision and cone vision are equally affected by oxygen deprivation.

The anomaloscope is probably the most delicate instrument for testing color vision. The subject adjusts mixtures of red and green to match yellow. The tendency to require a large proportion of green ("red sightedness") is called deuteranomaly; the converse ("green sightedness") is entitled protanomaly. Each is a form of anomalous trichromatism. The range of settings of red and green which appear to match yellow is also considered a measure of the integrity of the color sense. The anomaloscope was employed by Velhagen (1935, 1936) and by Schmidt (1937), who used somewhat different procedures and arrived at different conclusions.

Velhagen described what he called "hypoxemic color-blindness, a latent disturbance of the color sense." He stated that a large percentage of persons who have completely normal color vision at normal atmospheric pressure suffer a disturbance during oxygen deprivation closely resembling congenital anomalous trichromatism. In such persons there was found a widening, increasing with altitude, of the range of red-green mixtures which appeared to match yellow. Furthermore, according to Velhagen slight anomalies may become accentuated at a low tension of oxygen, and one form of congenital anomaly may be converted into another. This "hypoxemic color-blindness" was reported to be demonstrable at 3,000 meters (about 10,000 feet) and to disappear when oxygen was administered.

Schmidt stated that if there is no color blindness at sea level then altitude does not affect the integrity of the color sense. But if color blindness is present in normal air then as a rule it is increased by low pressure, usually at about 10,000 feet (about 3,000 meters). It may, however, remain unaltered or fluctuate. Contrary to Velhagen's findings, a pure "hypoxemic color-blindness" which becomes manifest only at low pressure without being at all demonstrable at sea level was not observed.

Moreover, there was no conversion of one form of anomaly into another. The author pointed out inadequacies in Velhagen's procedure which led to some of his "erroneous" conclusions.

6. *After-Images*.—Aviators and mountaineers have frequently mentioned the increased latency and unusual quality and intensity of the after-image at high altitudes. The latency of the negative after-image was investigated by Gellhorn and Spiesman (1935). Their subjects fixated colored squares or a white light for ten seconds, after which they closed their eyes and the latent period was measured with a stopwatch. Whereas a reduction of the oxygen concentration to 13 per cent was without effect, considerable changes occurred after air containing 9 to 11 per cent oxygen was breathed for various times (seven to twenty-

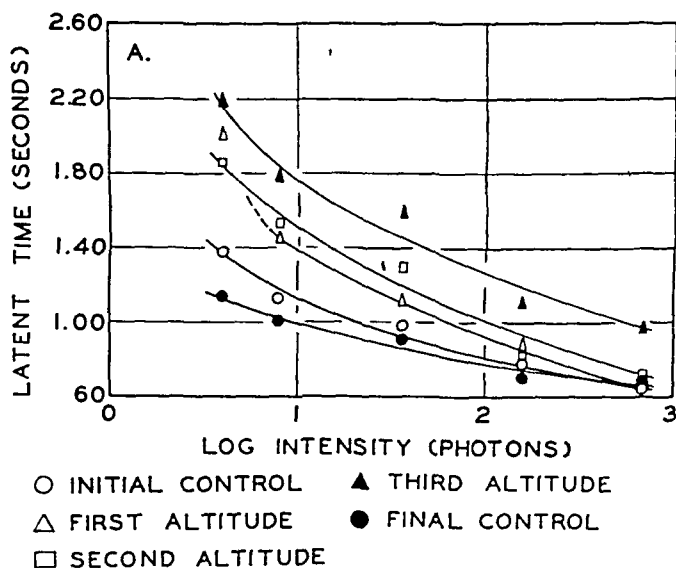


Fig. 5.—Latent time of the visual after-image as a function of intensity at low tensions of oxygen. The latent times of the after-images (in seconds) are plotted vertically and the intensity measured in photons horizontally. Each curve (fitted by visual inspection) indicates that the latent time decreases with an increase in intensity. In general an increase in anoxia produces a lengthening of the latent time of the after-image. The control tests were made while the subjects inhaled normal air. The anoxia tests were made while the subjects inhaled air with lowered concentrations of oxygen simulating those at the following altitudes: first altitude, 11,150 feet (about 3,400 meters); second altitude, 14,000 feet (about 4,200 meters), and third altitude, 17,000 feet (about 5,100 meters). (From McFarland, Hurvich and Halperin, 1941.)

seven minutes). The latent period was either considerably lengthened or became infinite, since the after-image failed to appear. In cases in which a negative after-image did appear the subject noticed a decrease in its intensity. In some cases the latent period remained lengthened even ten minutes after the end of the breathing period.

In subjects acclimatized to a high altitude on the international High Altitude Expedition to Chile, McFarland (1937), using a method similar to that previously described, also found a lengthening of the latent period, which was statistically significant at 20,100 feet (about 6,100 meters). There was a tendency for the after-image to persist longer. Several subjects reported qualitative variations, especially in brightness and hue of the after-image.

McFarland, Hurvich and Halperin (to be published) have recently made a systematic study of the behavior of the visual after-image during exposure to anoxia in a low oxygen chamber. Employing a wider range of stimulus intensities and relatively shorter stimulus durations than those used in the earlier studies, they found an apparent lengthening of the latent time of the after-image. In general, under conditions of oxygen deprivation the functions relating the latent time of the after-image to the stimulus intensity were displaced throughout the entire intensity range (fig. 5). On the whole the effects seemed to be more pronounced in the lower intensity range. This finding is in accord with the results obtained by McFarland and Halperin in the study of visual acuity in relation to oxygen deprivation. The data on the after-image also indicated that the recovery following the administration of oxygen was much slower than that in the case of the other visual processes studied.

7. Flicker Fusion Frequency.—The critical fusion frequency for flickering light was studied by Seitz (1940). His experiments were carried out in a low oxygen chamber. His apparatus was essentially a variable light source interrupted by a rotating sector disk. The rotational velocity of the disk (hence the flicker frequency) could be controlled and measured. The range of intensities studied was about 4 logarithmic units, or 1 to 10,000.

Oxygen deprivation equal to that at 17,500 and 20,000 feet (about 5,300 and 6,000 meters) was found to reduce the critical fusion frequency in the intensity ranges corresponding to both rod function and cone function. The entire curve relating fusion frequency to illumination was displaced. The data do not extend over a sufficiently wide range of stimulus intensities, however, to make clear whether the shift was only along the intensity axis (as in the case of visual acuity) or along both axes.

Experiments were also done in which an extended series of readings was obtained at each of two fixed intensities. These were chosen so that one involved principally the rods and the other the cones. During about one and one-half hours of exposure there was no evidence of improvement which might be attributable to acclimatization. Seitz found a slightly greater effect on the cones than on the rods at these intensities. Numerous studies, including the one being discussed, have, however,

shown that the degree of change produced by anoxia on various functions of the rods and of the cones varies with the stimulus intensity. Therefore, it cannot be concluded that cone function in general suffers more from anoxia than does rod function. As has already been mentioned, dark adaptation studies have shown that anoxia produces approximately equal changes in what has been interpreted as rod function and as cone function.

Local application of strychnine solution to the conjunctiva resulted in a diminution or complete cancellation of the effects of anoxia. This conforms with the results of similar studies on the angioscotoma.

8. *Intraocular Tension*.—No alteration in intraocular tension was noted by Wilmer and Berens (1918). Goldmann and Schubert measured the tension in 2 of their subjects and found no change. Recently Pinson (1940) measured the intraocular tension of anesthetized rabbits directly with a capillary mercurial manometer during environmental pressure changes equivalent to those experienced at rates of ascent and descent of 1,000 to 30,000 feet (about 300 to 9,000 meters) per minute to altitudes up to 40,000 feet (about 12,000 meters). These environmental pressure changes "produced no alterations in the intra-ocular pressure sufficient to cause concern as to any injury or discomfort to the eye," being less than the usual variations of intraocular pressure which occur with the cardiac and respiratory cycles in rabbits.

On the other hand, Furuya (1936) found that the ocular tension always increases at altitudes above about 13,000 to 16,000 feet (about 4,000 to 4,800 meters). He made measurements on 6 subjects in a low pressure chamber. The effect was more marked in sympathicotonic than in vagotonic persons. During continued exposure at a given altitude the tension tended to recede toward its original value. Immediately after "descent" the tension dropped further, and it then rose to its original level in about thirty minutes.

Similar findings were reported by Buscalossi (1938), who measured with a Schiötz tonometer the ocular tension of subjects exposed to low pressure in a chamber. The ocular tension underwent changes similar to those of the arterial pressure. It increased during the simulated ascent and then decreased toward its original value during maintenance of the low pressure for fifteen minutes. No noticeable variation occurred during "descent." The amount of elevation of the ocular tension was proportionate both to the "altitude" reached and to the rate of "ascent" and was of an order of magnitude of several millimeters of mercury.

9. *Extraocular Muscles*.—Velhagen (1936), using the Stock photometer, made low pressure chamber experiments on 16 subjects with slight esophoria or exophoria. He found that for distant vision there was a displacement of the rest position of the eyes in the direction of

latent esophoria beginning at about 10,000 feet (about 3,000 meters). This was independent of previous esophoria or exophoria. For near vision (25 cm.) the results were not so consistent but there appeared to be an insufficiency of convergence—a tendency toward exophoria. The author suggested that there must be some alteration in the muscle itself rather than in the central nervous system.

McFarland (1937), reporting his observations on 10 acclimatized subjects during the International High Altitude Expedition to Chile, stated that no significant alterations in heterophoria at 6 meters were found even at 20,000 feet (about 6,000 meters). On the other hand, the test for 40 cm. vision revealed an increase of the average deviation from orthophoria, usually in the direction of an insufficiency of convergence. This was already measurable at 9,200 feet (about 2,800 meters). The mean rose from 1.5 prism diopters at sea level to 6.7 prism diopters at 20,000 feet. In experiments in a low oxygen chamber McFarland (1938) found similar changes. In his study the alterations in the phorias were statistically reliable only at altitudes of 14,000 feet (about 4,200 meters) and above.

In commenting on a paper by Sauer (1924), Weldon made the following interesting statement:

Diplopia is caused by lowered O_2 -tension only in those cases in which there is latent squint—heterophoria. This double vision, and when it comes on it is a frank and uncontrollable double vision, may develop at any altitude over 10,000 feet. It is particularly liable to occur in one having hyperphoria. . . . The amount of hyperphoria need not be large, because at sea-level conditions these cases have good binocular fixation. It is held with extra effort, however, and in high altitude with its consequent low oxygen supply, this extra effort is not available and diplopia results.

Wilmer and Berens (1918) found a decrease in adduction, abduction and sursumvergence of 1.90, 1.55 and 1.25 degrees, respectively, at 20,000 feet (about 6,000 meters). They stated that exophoria or hyperphoria is much more serious than esophoria. They measured the field of binocular fixation in a group of men with normal muscle balance and in a group with heterophoria. They found that whereas only 7 per cent of the former group suffered deterioration during anoxia 50 per cent of the latter group suffered a contraction. In tests with a stereoscope there was a change in fusion ability in 2 of 6 persons with normal muscle balance and in 1 of 3 with subnormal balance.

10. *Accommodation and Convergence.*—Wilmer and Berens (1918) found that the near point of accommodation and of convergence receded during rebreather tests. This occurred in about half of their 148 subjects; about one fifth of them improved, and in the rest the near points remained unchanged or fluctuated.

A study of 6 subjects by Furuya (1937) resulted in his finding a decrease in range of accommodation which began above 5,000 meters (16,400 feet). Continued exposure to the same pressure was followed by further impairment. It required forty minutes after return to normal pressure before the effects of a sixty minute sojourn at 5,000 meters were overcome.

Measurements of fatigue of accommodation and of convergence were also made by Wilmer and Berens, using the Howe (Berens) ocular ergograph. They found increased fatigability at 15,000 and 20,000 feet (about 4,500 and 6,000 meters). Employing a similar technic in the Andes, McFarland (1937) found that in acclimatized subjects the fatigue during a ten minute run on the ergograph was not significant at 9,200 feet (about 2,800 meters). However, at the highest stations (15,500 and 17,500 feet, or about 4,700 and 5,300 meters) it was increased significantly for both accommodation and convergence.

11. *Coordinated Ocular Movements.*—The effects of oxygen deprivation on ocular movements during reading and during fixation have been studied with photographic technics by McFarland, Knehr and Berens (1937 a). Persons with normal visual acuity and muscle balance as well as patients with excessive heterophoria or even heterotropia combined with lowered visual acuity were used as subjects. A beam of light reflected from the cornea of the eye was recorded on a moving film while the subject was reading printed lines from the page of a book or while fixating on a target. The object of the study was not only to analyze the effects of anoxia on an unconscious and well established motor habit but to study the basic mechanisms involved in reading and in ocular motor anomalies. A typical record of the effects of anoxia on the ocular movements of a subject with normal vision is shown in figure 6 A. The results showed not only that it took longer to read a given line but also that the eyes did not coordinate so well at 18,000 feet (5,400 meters, 10.5 per cent oxygen), as shown by the lack of parallelism between the two ocular tracks of figure 6 B. There was a general tendency toward diminished precision of the ocular fixation. In a number of subjects with seemingly normal ocular muscle balance certain latent defects were made apparent with low oxygen pressure.

In the second study of ocular movements (1937 b) a series of patients with known ocular anomalies were exposed to lowered tensions of oxygen. The defects were greatly accentuated during anoxia. In 1 subject, for example, fusion occurred during fixation on a test object but during reading there was suppression of one image and not always in the same eye. This phenomenon was greatly accentuated with a low oxygen tension. In all the 10 patients there was a diminution in the precision of the ocular reactions, with the appearance of nystagmoid movements, general unsteadiness and accentuation of abnormalities. An

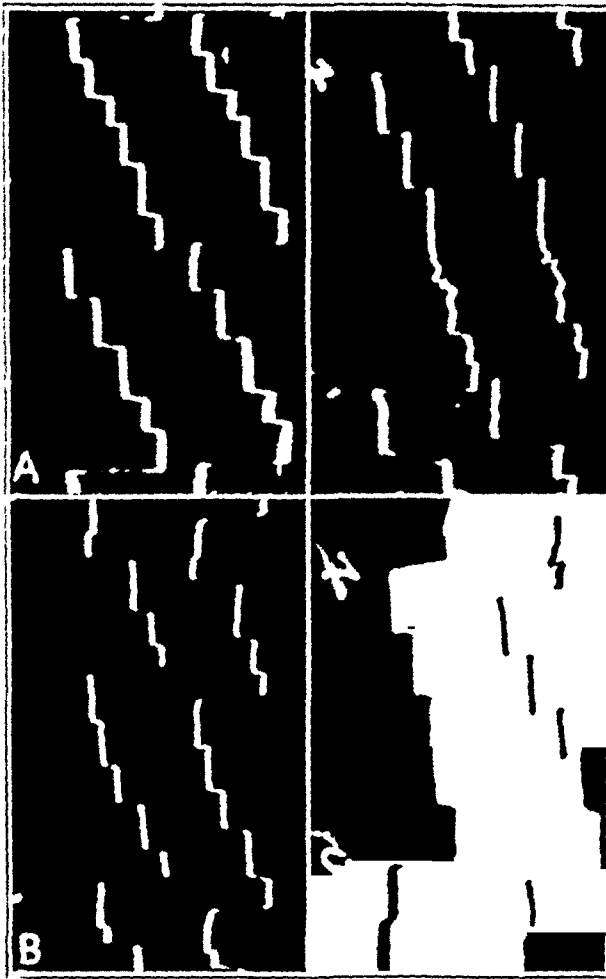


Fig. 6.—The ocular movements during reading. The photographs show the corneal reflections of beams of light from the two eyes on a moving film while the subject was reading printed lines from a book. The stepwise phenomena represent ocular fixations during the reading of a line. The fixations vary in number from four to ten according to whether the subject is a slow or fast reader. *A*: The control record, at the left, obtained while the subject was breathing normal air, is very regular, with five to six ocular fixations to each printed line; the record on the right, however, obtained with the subject breathing air containing 10.5 per cent oxygen, simulating that at 18,000 feet (5,400 meters), shows a larger number of fixations and marked unsteadiness. *B*: The control record, at the left, was obtained while the subject was inhaling normal air; the one at the right, obtained while the subject was breathing air containing 10.5 per cent oxygen, is very irregular. There is a gradual increase in the distance between the ocular tracks, indicating an increasing convergence. The ocular movements at a low oxygen tension revealed in a striking fashion the hyperphoria on the left. (From McFarland, Knehr and Berens, 1937 *a*.)

illustration is shown in figure 7, a reproduction of the corneal reflections from the eyes as recorded on a moving film while the subject was fixating on a test object. The record at the left was obtained while the subject was breathing normal air and the one at the right in a low oxygen chamber with an oxygen concentration simulating that at 16,000 feet (4,800 meters; 11.25 per cent oxygen). The anoxia tended to bring out the divergence excess in the patient's ocular movements; also, the nystagmoid movements became marked.

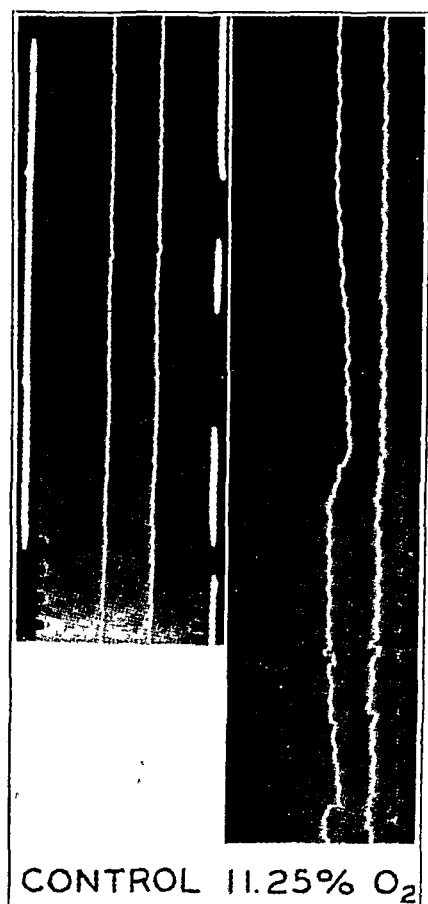


Fig. 7.—Reproductions of photographs of the ocular movements while the patient was fixating on a test object. The photographs show the corneal reflections of beams of light from the two eyes on a moving film while the subject was fixating on a stationary test object. The record at the left was obtained while the subject inhaled normal air and the one at the right while he inhaled air containing 11.25 per cent oxygen, simulating that at 16,000 feet (about 4,800 meters). The divergence excess of this patient was clearly manifest during steadiness fixation under anoxia. Note how the gradual divergence is followed by fusion and how the nystagmoid movements are marked at a low tension of oxygen. (From McFarland, Knehr and Berens, 1937 *b.*)

In analyzing the data from the two studies discussed, the authors found no general correlations between the results of ocular examinations and the records of ocular movements obtained while the subjects were breathing low oxygen mixtures. When the photographic records were analyzed individually, however, significant changes were observed which could be related to the results of the clinical examinations. The authors concluded that a photographic record of ocular movements during reading or during fixation on a test object if obtained while the subject is exposed to anoxia is of value in the diagnosis of clinical anomalies. The method has the advantage of providing an objective record of the movements of the eyes during a normal act, such as reading. Furthermore, they suggested that records obtained during the breathing of low oxygen mixtures are of clinical significance owing to the fact that latent defects not previously observed became apparent and those known to be present are accentuated in such a way as to be more easily diagnosed.

V. SUMMARY

No attempt will be made to summarize in detail the results of these studies of ocular functions carried out under conditions of anoxia simulating the oxygen want that exists at high altitudes. So many different technics have been used that brief generalizations can be made only at the expense of accuracy. In fact, one must employ qualified and descriptive statements in order to make clear and to compare the findings of the various investigations. If this is borne in mind, however, the following tabulation of the experimental findings on the effects of acute anoxia on ocular functions may be of some value.

1. Light sense (visual sensitivity):
 - (a) The light minimum (absolute threshold) is impaired.
 - (b) Dark adaptation is impaired.
 - (c) The studies relating to light difference (differential sensitivity) are inadequate.
2. Visual acuity (foveal): It is decreased in dim light but practically unaffected in bright light.
3. Peripheral visual fields: The studies are inadequate thus far.
4. Central visual fields: They are decreased by widening of the angioscotoma.
5. Color zones: The studies are inadequate thus far.
6. Color vision: It is apparently further impaired if abnormal prior to anoxia.
7. After-image: The latent period is prolonged.
8. Eyegrounds: The diameters of the arteries and of the veins are increased about one eighth.
9. Extraocular muscles: Weaknesses become significantly exaggerated.
10. Accommodation: The range of accommodation is decreased.
11. Coordinated ocular movements: The ocular motor reactions, such as those employed in reading, are less orderly, and latent defects become apparent.
12. Ocular fixation: There is a diminished precision in fixating on test objects, and motor anomalies become accentuated.

VI. CONCLUSIONS

A number of general observations might be mentioned in the light of this review. In the first place, although a great amount of work has been done many defects exist in the knowledge of the subject. Certain of the studies should be repeated with standard apparatus designed to record more accurately. The research should be repeated under conditions both of acute and of chronic anoxia with normal subjects as well as with patients suffering from various ocular anomalies. Also, the effects of excesses of carbon dioxide and of high concentrations of oxygen should be analyzed more thoroughly in normal subjects and in clinical patients with various known defects, especially those in which impaired oxidation might be involved. Secondly, the method offers promise not only because of the fundamental role of oxidation in all the tissues of the body but especially because of the fact that the eye, being essentially an extension of the brain, is known to be especially sensitive to anoxia. It is possible that a clearer understanding of certain visual defects might be revealed by exposing patients to excess and to deficient concentrations of oxygen. Latent defects are sometimes revealed by such procedures. Also, knowledge of the fundamental nature of certain visual mechanisms may be extended. Thirdly, many of the studies discussed in this review suggest that the basis for theories should be broader in regard to the nature of certain visual functions. A case in point is the fact that photochemical theories of vision appear to have definite limitations. A broader viewpoint is forced on one, including that of the important role of central processes, i. e. the central nervous system or the brain. Fourthly, the practical importance in aviation of such studies is apparent. In modern aerial warfare definite strategic advantage may be obtained by a more thorough knowledge of visual acuity and night vision at high altitudes and of the variables involved. The applications to diseased conditions, local and systemic, are not so direct but are none the less promising. Finally, it should be emphasized that there are many opportunities for original research in this field. Oxygen is so basic a substance in all biologic functions that the effects of marked variations in ocular functions cannot help but reveal important data for the ophthalmologist.

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Correspondence

"A COLOR STEREOSCOPIC PHENOMENON"

To the Editor:—Probably Dr. Loewenstein and Dr. Donald would not have written their paper, "A Color Stereoscopic Phenomenon," which appears in your October issue (ARCH. OPHTH. 26: 553, 1941) if they had run across my much shorter paper of thirteen years ago (Verhoeff, F. H.: An Optical Illusion Due to Chromatic Aberration, *Am. J. Ophth.* 11: 898, 1928). I not only described the phenomenon about which they speculate but pointed out features of it which they overlook or misunderstand. Moreover, I clearly demonstrated that it is dependent on two optical factors, chromatic aberration and eccentricity of the lens system, while they attribute it in great part to some obscure psychologic cause. I also pointed out that the eccentricity can be provided by artificial means when, as is sometimes the case, a person does not possess a sufficient amount of it to permit him to observe the phenomenon. This fact seems to be unknown to Dr. Loewenstein and Dr. Donald, if only because they are unaware that such an optical defect has anything to do with the phenomenon. In considering their psychologic experiments, two facts should be kept in mind. One is the familiar fact that a large circle and a much smaller circle within it even when viewed binocularly can appear as they actually are or as a truncated cone pointing sometimes toward and sometimes away from the observer. The other fact is that when the definite appearance of such a cone is produced by means of a stereoscope or when an actual truncated cone is viewed binocularly, the stereoscopic effect cannot be reversed by a sane observer even when he exercises his strongest imagination. Although nothing that I said in my paper has been refuted, I was informed shortly after its publication that the phenomenon had previously been described in the literature and an explanation given similar to mine. However, I did point out important facts not previously known, which evidently even now are not widely known.

F. H. VERHOEFF, M.D., Boston.

News and Notes

UNIVERSITY NEWS

Dinner for Dr. John E. Weeks.—A dinner in honor of Dr. John E. Weeks, professor emeritus of the department of ophthalmology of New York University College of Medicine, was held at the Union Club, New York City, October 6. Eighty of Dr. Weeks's friends and students attended. The speakers' program was as follows: "The Development of the Laboratory Side of Ophthalmology," Edgar Burchell, Sc.D.; "Undergraduate Ophthalmology in Relation to the General Medical Course," Dr. Currier McEwen, dean, New York University College of Medicine; "Graduate and Postgraduate Courses in Ophthalmology," Dr. John H. Dunnington, professor of ophthalmology, Columbia University College of Physicians and Surgeons; "The Relation of the Special Hospital to the University or General Hospital," Dr. David H. Webster, executive surgeon, Manhattan Eye, Ear and Throat Hospital; "The American Board of Ophthalmology," Dr. Conrad Berens, chairman, American Board of Ophthalmology, and "The Chair of Ophthalmology of New York University College of Medicine," Dr. John E. Weeks. Dr. Daniel B. Kirby, professor of ophthalmology, New York University College of Medicine acted as toastmaster.

In 1923 Dr. Weeks received the special degree of Doctor of Law from New York University.

The Eye Surgery Fund, Inc., a foundation for the training of ophthalmic surgeons and for the alleviation of blindness, was dedicated to the memory of Dr. Webb W. Weeks. The poem "Spring and the Blind Children" has been dedicated to this foundation by the author, Alfred Noyes. Two of the stanzas follow:

They passed the primrose glistening in its dew,
With empty hands they drifted down the lane,
As though, for them, the Spring held nothing new;
And not one face was turned to look again.

Like tiny ghosts along their woodland aisle
They stole. They did not leap or dance or run;
Only at times without a word or smile
Their small blind faces lifted to the sun.

SOCIETY NEWS

Society of Ophthalmology of Córdoba.—A special meeting of the Society of Ophthalmology of Córdoba, Argentina, was held on August 16 in the Medical Circle with the object of bringing about a better understanding and of creating friendship between the several ophthalmologic societies of Argentina and of other countries in South America. The meeting was prompted by Prof. Carlos Weskamp.

Prof. Urrets Zavalía introduced the visiting physicians. The following papers were read: "The Macular Serosa in Chorioretinitis," Prof. Carlos Weskamp; "Medicolegal Problems," Dr. J. M. Vila Ortiz; "The Stenopaic Disk in Refraction," Dr. Isaac Cotlier, and "The Stereoroentgenogram in Ophthalmology," Professor Carlos Weskamp.

Great interest was shown in the presentations and especially in that concerning the macular serosa in chorioretinitis.

The following physicians, among others, were present: Profs. Carlos Weskamp and Uretts Zavalía and Drs. Brandan, Vila Ortiz, Laje Weskamp, Remonda, Obregon Olivia, de Anquin, Ponce de Leon, Maffrand, Di Pinto, Richardson, Joisen Pelliza, Paez Allende and Wolaj. Many students also were present.

CORRECTION

In the news note in the July issue (ARCH. OPHTH. 26: 131, 1941) on the fourth Brazilian Congress of Ophthalmology, held in Rio de Janeiro June 26 to July 1, the name of Dr. Jacques Tupinamba, president of the São Paulo Society of Ophthalmology, was omitted. Dr. Tupinamba was one of the representative ophthalmologists of the state of Brazil who attended the congress.

Abstracts from Current Literature

EDITED BY DR. WILLIAM ZENTMAYER

Cornea and Sclera

BILATERAL (MESIAL) DEFICIENCY OF THE SCLERA: SCLERAL PLAQUES.
B. GRAVES, Brit. J. Ophth. 25: 35 (Jan.) 1941.

The patient was a woman of 70 who showed scleral plaques of unequal depth on the temporal side of each cornea. The nasal (mesial) aspect of the scleras revealed no plaques, but optical sections of the surface of each eye revealed some flattening (or even slight concaving) in a small area. Graves proposes to drop the term he first used and to use Cutler's term scleral plaques as more suitable.

He reports this case of scleral plaques principally to show that the qualifying term mesial, which he originally used, must be dropped, though it would seem that scleral plaques are much more common on the nasal side of the sclera than elsewhere.

The article is illustrated.

W. ZENTMAYER.

EPIDEMIC KERATOCONJUNCTIVITIS. R. SCHEERER, Klin. Monatsbl. f. Augenh. 105: 110 (July) 1940.

Like other writers, Scheerer found that the period of incubation of epidemic keratoconjunctivitis is a week, particularly when the condition develops in connection with a foreign body in the cornea. Corneal complications appear after another week. Visual disturbances as a rule disappear more or less completely even in the presence of central corneal opacities. Irradiation with skin erythema doses of 100 roentgens at an early stage of the disease proved its merits. When this treatment is late for the first eye, corneal efflorescences may be entirely prevented in the second eye if it is begun at the onset of conjunctival irritation.

K. L. STOLL.

APPLICATION OF COD LIVER OIL TO BURNS OF THE EYE. V. A. TIKHOV, Vestnik oftal. 17: 396, 1940.

Tikhov used several daily instillations of cod liver oil in treating burns of the cornea caused by sulfuric acid, caustics, lime, metal or steam. There were many second degree burns. The results were favorable; the pain was lessened considerably, epithelization of the cornea was quick, the opacities were not dense and the vision was better than was to be expected in view of the severity of the process.

O. SITCHEVSKA.

General Diseases

NEW ENDEAVORS IN THE BATTLE AGAINST OCULAR TUBERCULOSIS.
W. WEGNER, Klin. Monatsbl. f. Augenh. 104: 395 (April) 1940.

In referring to the papers of Stromburg and Hallermann in the same issue, the author mentions that their views and his own are

based on the work of Axenfeld between 1900 and 1930. The reports on successful cures of ocular tuberculosis are misleading and too optimistic, because the period of observation was usually too short. Ocular tuberculosis is the most frequent cause of blindness. Wegner studied 2,000 patients with about 3,000 diseased eyes. Certainty as to success or failure of the treatment can be obtained only after observation lasting twenty to thirty years. Stromburg stressed this fact. Wegner points out that patients with ocular tuberculosis are sick. Irritation of a climatic or pharmaceutic nature must be avoided, and sunlight, even, must be employed carefully. He refers in this connection to a patient with a severe toxic-tuberculous lesion of the macula lutea caused by sunburn of the skin. Recurrences of tuberculosis are known to develop slowly and stealthily, and patients will not notice or will disregard the onset. Wegner therefore recommends that patients present themselves for examination at regular intervals. His suggestions to this end were accepted by the agencies for social insurance and governmental insurance for employees in Germany. K. L. STOLL.

Hygiene, Sociology, Education and History

OCULAR FACTORS IN POOR READERS IN THE SAINT LOUIS PUBLIC SCHOOLS. F. O. SCHWARTZ, *Am. J. Ophth.* 23: 535 (May) 1940.

This article does not lend itself to abstracting. It is a study of the eyes of 1,109 children who were the poorest readers in a number of schools. A second survey indicated that 70.7 per cent made progress as a result of recommendations made after the first study.

W. S. REESE.

DEVELOPMENT OF MODERN OPHTHALMOLOGY IN ONE LIFETIME. E. JACKSON, *Am. J. Ophth.* 23: 759 (July) 1940.

This is the first "de Schweinitz lecture" delivered before the Section on Ophthalmology of the College of Physicians of Philadelphia. In it are considered the changes in ophthalmology that occurred during the lifetime of George E. de Schweinitz.

W. S. REESE.

Methods of Examination

EVALUATION OF MANTOUX TUBERCULIN TEST WITH HUMAN AND BOVINE TUBERCULIN IN OCULAR DISEASES WITH SPECIAL CONSIDERATION OF THRESHOLD REACTION. H. SCHLICHTING, *Klin. Monatsbl. f. Augenh.* 104: 401 (April) 1940.

In discussing the value of the diagnostic tuberculin test, Schlichting points out some errors and uncertainties connected with it. With two exceptions the subject is free from tuberculosis if the test shows no evidence even with a large dose. The reaction will not show positive results until several weeks after a tuberculous infection. Sensitivity to tuberculin may be greatly reduced or even eliminated in patients with advanced tuberculosis in the presence of measles, croupous pneumonia, scarlatina, epidemic meningitis, grip, typhoid fever, pertussis or varicella

and after therapeutic injections of tuberculin. A positive reaction to tuberculin is proof that the subject is infected with tuberculosis but not that he is sick. Schlichting discusses the value of the intercutaneous test with tuberculin and adds a number of tables. Intracutaneous injections of human or bovine tuberculin were given to 87 persons suspected of having ocular tuberculosis and 87 healthy controls. The weakest solution of tuberculin which elicits a reaction was used. No essential difference in action was found between human and bovine tuberculin. The reaction in persons suspected of having tuberculosis and that in healthy persons showed no important difference. As a rule the actually tuberculous patient showed a negative reaction or a positive reaction only to a high concentration. The intracutaneous reaction to tuberculin therefore appears to be unreliable as a test of the possible tuberculous nature of an ocular disease.

K. L. STOLL.

Neurology

OCULAR COMPLICATIONS OF MENINGOCOCCIC MENINGITIS. P. M. LEWIS, *Am. J. Ophth.* 23: 617 (June) 1940.

Lewis gives the following summary of his study:

"The eyes of 350 patients with meningococcic meningitis have been examined over a period of nine years. Repeated examinations were made when indicated. The findings of numerous other observers are given as well as those of the author. Each structure of the eye is considered separately and its complications described. Any of the structures of the eye may be involved, and very occasionally all are affected. In this series of 350 cases, 44 percent showed some deviation from the normal. Deducting 14 percent, which showed only an engorgement of the retinal veins, there remain 30 percent with definite pathologic changes. The most frequent complication in this series was papillitis. Papilledema was quite rare.

"Metastatic endophthalmitis was the most spectacular and also the most disastrous complication. Photomicrographs of several eyes enucleated for endophthalmitis, with a brief description of the pathologic findings, have been included.

"The modern treatment of meningococcic meningitis by antitoxin and sulfanilamide is recommended, but not described in detail. Frequent ocular examination of all cases is urged."

W. S. REESE.

EYE STUDIES FOLLOWING LUMBAR PUNCTURE. L. S. POWELL and H. S. SMITH, *Am. J. Ophth.* 23: 792 (July) 1940.

Powell gives the following summary of his investigations:

"When small amounts of spinal fluid were withdrawn in the manner outlined, the following observations were made on 56 apparently physically well individuals.

"1. No appreciable change following lumbar puncture was seen in visual acuity, intraocular tension, or blood pressure.

"2. Pathological changes in the eye, including edema and hyperemia of the disc, were observed in 16 of the 56 cases.

"3. Changes in the optic disc were associated with nausea and headache in only 9 of the 16 cases."

W. S. REESE.

DIAGNOSIS AND THERAPY OF TUMORS IN REGION OF CHIASM.
P. KNAPP, *Klin. Monatsbl. f. Augenh.* 105: 402 (Oct.) 1940.

The author reviews the anatomy, physiology and topography of the hypophysis and the pathologic processes influencing the chiasm. Tumors in the region of the chiasm are discussed with reference to the differential diagnosis, external changes, intraocular symptoms, field of vision and roentgenologic data. Related conditions, such as arachnoiditis, Foster Kennedy's syndrome and Simmons' cachexia are discussed, and the importance of the relation between the hypophysis and the midbrain is stressed. Valuable hints are given relative to the therapy, roentgenologic and surgical. The hypophysis exerts a dominant role in the endocrine system by regulating the sexual system and the metabolism of lime, fat and carbohydrate. In addition, it forms a functional entity with the nervous centers of the midbrain: This explains why pathologic processes in either organ produce similar symptoms. When suspecting a tumor of the hypophysis one must remember that widening of the sella turcica and bitemporal hemianopsia may be due to bulging of the third ventricle caused by a tumor or internal hydrocephalus and that even a remote tumor of the brain may cause changes in the sella turcica by increased intracranial pressure. Since choked disk occurs rarely in association with an intrasellar tumor, it would count against the presence of such a tumor, but simple atrophy of the optic nerve by pressure is the rule.

Choked disk develops more frequently with the appearance of a suprasellar neoplasm. Of therapeutic importance is the fact that chromophilic (acidophilic and basophilic) adenomas of the hypophysis usually respond well to roentgen irradiation, whereas chromophobe forms, meningiomas and tumors of the duct of the hypophysis, respond but slightly or not at all. Irradiation may be successful even in the treatment of a malignant or unclassified tumor. It should be employed first in most cases and surgical measures resorted to after it has failed, when dangerous symptoms arise or when the vision and the field of vision deteriorate rapidly.

K. L. STOLL.

OCULAR SYMPTOMS OF MALIGNANT TUMORS OF THE RHINOPHARYNX.
E. GODTFREDSSEN, *Acta ophth.* 18: 336, 1940.

Between 1931 and 1940, 64 patients with malignant tumors of the nasopharynx were observed at the radium station in Copenhagen, Denmark. Twenty showed ocular complications.

Characteristically, tumors in this region, which may be sarcoma, carcinoma or endothelioma, occur in relatively young persons. The deep cervical nodes may be involved by extension through the lymphatics while the tumor remains small. Compression of the cervical sympathetic nerve by these nodes may produce Horner's syndrome. Growth of the tumor upward, through the foramina in the base of the skull, may lead to involvement of any of the nerves supplying the eye. The 20 patients had fifty lesions of the ocular nerves.

In the author's series roentgen therapy exerted favorable effects. In 1940, 7 patients were alive and had been free from symptoms for from

six months to seven years. Thirteen died in from seven months to five years after the first appearance of symptoms. Of these, 6 had periods of transitory improvement varying from two months to three years.

O. P. PERKINS.

Ocular Muscles

CONVERGENCE. M. DOBSON, *Brit. J. Ophth.* 25: 66 (Feb.) 1941.

Dobson considers the subject of convergence under the headings of physiologic exophoria and diagnosis of convergent imbalances. Of the various tests used to investigate the presence of insufficient or excessive convergence, the cover test is perhaps the most accurate. The prism stereoscope test is reliable for estimating convergence stability at the reading distance. If duction reserves are normal, many imbalances cause no symptoms whatever.

The treatment of heterophoria is outlined, and a number of practical suggestions are made.

W. ZENTMAYER.

THE MEASUREMENT OF HETEROPHORIA. N. CRIDLAND, *Brit. J. Ophth.* 25: 141 (April) 1941.

According to the author, the purpose of this paper is to collect, in some measure to collate and occasionally to assay the literature of seventy years. Having done this, he summarizes, of necessity dogmatically, the conclusions reached.

"(1) There are four positions of rest of the eyes; each is the result of additional factors operating upon its predecessor.

"(2) The anatomical position of rest is the resultant of all anatomical and non-nervous physiological factors and, in the absence of secondary pathological changes, it is, invariably, divergence.

"(3) In the physiological position of rest is added the effect of minimal, balanced, tonus of all the extra-ocular muscles. It is closely akin to the anatomical position of rest.

"(4) The physiological position of rest is changed into the fusion-free position by the addition of the effects of the postural and fixation reflexes.

"(5) The functional primary direction is visual parallelism.

"(6) According to the test employed, and the care given to the ancillary conditions, the position of rest revealed by any test for heterophoria may be the fusion-free position, or some position intermediate between this and the physiological position of rest, or any perversion of either of these. The physiological position of rest is not obtained by any practicable test yet devised.

"(7) Basic heterophoria is the latent tendency of the eyes in vision at infinity to deviate from the functional primary direction, in the presence of actual or effective emmetropia.

"(8) The criteria of efficiency of a test for heterophoria depend on the position of rest which it is desired to obtain. Since, for most prac-

tical purposes, the fusion-free position is required, the fusion reflex is to be excluded, and the postural and fixation reflexes are to be stimulated in such ways only as will not cause a false deviation of the visual axes.

"(9) 'There are many ways of so stimulating the postural or fixation reflexes or both as to cause a deviation which vitiates the measurement of a heterophoria. The majority of tests are open to damaging criticism on these grounds.

"(10) The wearing of glasses for a test is insufficient, for they must have been worn previously for long enough to have re-established a normal accommodation-convergence ratio. With this precaution, the use of a cycloplegic is unnecessary.

"(11) The deviation must be given time to develop; generally speaking, enough time has been given when two successive measurements are the same.

"(12) The range of variations of the deviation can, with care, be made small enough to render a single measurement significant."

The article is to be concluded.

W. ZENTMAYER.

Operations

EXTERNAL SCLERAL INCISION IN A SHALLOW ANTERIOR CHAMBER.
A. POKROWSKY, *Vestnik oftal.* 16: 295, 1940.

The external scleral incision is advocated as the best approach to the angle of the anterior chamber, to the base of the iris for iridectomy and to the iris for removal of anterior and posterior synechias. The operation is simple and can be done by an inexperienced surgeon. There is no danger of injuring the lens; the uneven scar of the sclera renders it less rigid, which is valuable in the case of glaucoma. With a scalpel perpendicular to the surface of the sclera Pokrowsky makes an incision about 10 mm. long above the limbus. Whenever the iris did not appear in the wound he entered the anterior chamber, freed the adhesions and pulled out the iris with iris forceps.

Of the patients operated on, the majority (62) had secondary glaucoma due to leukoma, seclusion of the pupil or staphyloma; 14 had acute or chronic inflammatory glaucoma; 2 had fistula of the cornea, and an iridotomy was performed on the blind eye of 2 because of sympathetic ophthalmia and of 3 because of cysts of the iris in the anterior and posterior chambers of the eye. In 23 cases an iridectomy was done both for glaucoma and for optical purposes.

Of the cases of secondary glaucoma, the tension was lowered in 56 and the vision improved in about half. Normal tension and improvement of vision were obtained in the cases of prophylactic iridectomy. In the 2 cases of sympathetic inflammation the vision was improved. The removal of cysts of the iris was possible because of the external incision of the sclera, which made the anterior chamber accessible.

O. SITCHEVSKA.

Orbit, Eyeball and Accessory Sinuses

MALIGNANT EXOPHTHALMOS AFTER STRUMECTOMY. V. A. JENSEN, *Acta ophth.* 18: 1, 1940.

The author records the histories of 4 patients with exophthalmic goiter in whom malignant exophthalmos developed after partial thyroidectomy.

From a review of the literature it is concluded that this complication affects men more often than women and appears about nine months after operation on the thyroid. Characteristically, conjunctival hyperemia and epiphora are followed by pronounced proptosis, chemosis of the eyelids and conjunctiva and reduction of motility of the globe. Diplopia may occur as a result of mechanical interference with the function of an extraocular muscle, and vision may be affected by papilledema. The classic lid signs of Graefe, Moebius and Stellwag are absent. The basal metabolic rate is usually decreased by 10 to 20 per cent.

The origin of the condition is still unsolved, though animal experimentation indicates that abnormal activity of the anterior lobe of the hypophysis in the presence of a diminished function of the thyroid may be responsible.

The author advocates surgical intervention in the form of Naffziger's operation or Sewell's operation at the first sign of a corneal complication.

O. P. PERKINS.

Pharmacology

COMPARATIVE STUDY OF BENZEDRINE, PAREDINE, AND COCAINE WITH HOMATROPINE AS CYCLOPLEGICS. E. B. WEINMAN and F. B. FRALICK, *Am. J. Ophth.* 23: 172 (Feb.) 1940.

Weinman and Fralick conclude from their tests that a solution containing 4 per cent homatropine hydrobromide and 0.5 per cent cocaine hydrochloride in six instillations at ten minute intervals gives a residual accommodation of from 0.7 to 1.6 D. which lasts for several hours and allows a long period in which to complete the refraction. In many cases the solution causes dulness of the cornea, hindering retinoscopy. One insertion of a wafer containing $\frac{1}{50}$ grain (0.0012 Gm.) of homatropine hydrochloride and $\frac{1}{50}$ grain (0.0012 Gm.) of cocaine hydrochloride causes approximately the same degree of cycloplegia, but there is a foreign body sensation which cannot be completely relieved with pontocaine hydrochloride. Equally good cycloplegia is obtained with 1 drop of a solution containing 5 per cent homatropine hydrobromide and 1 per cent amphetamine sulfate but the cycloplegia is not lasting and the optimum time for refraction is fifty-five minutes, the eye returning to normal in eighteen hours. The pupil is widely dilated by this means, and the cornea remains clear and bright. A similar effect is obtained with a solution containing 5 per cent homatropine hydrobromide and 1 per cent paredrine hydrobromide (p-hydroxy- α -methylphenethylamine hydrobromide). This solution is said to be more satisfactory, as it does not cause an increase in the intraocular pressure, but the cycloplegia is slightly more prolonged.

W. S. REESE.

The Pupil

THE TABETIC PUPIL. P. W. LEATHART, Brit. J. Ophth. 25:111 (March) 1941.

Leathart gives the following summary of his article:

"1. The anatomy of the three primary ocular reflexes is described in detail.

"2. The characteristics of the tabetic pupil are enumerated.

"3. It is shown how it is almost impossible for a mid-brain lesion to produce pupils with the characteristics of a tabetic pupil without at the same time causing other physical signs.

"4. It is pointed out that a hypothetical lesion in the brachium of the superior colliculus of both sides produces pupils with all the characteristics of the tabetic pupil.

"5. It is postulated that such lesions are present in tabetics and are the cause of the Argyll Robertson pupil.

"6. A possible explanation of the fact that syphilitic poison destroys afferent fibers of posterior spinal roots and of the brachia of the superior colliculi is given.

"7. It is postulated that such lesions are present in tabes in the posterior roots and in the brachia of the superior colliculi and are the cause of absent knee and ankle reflexes and of the Argyll Robertson pupils respectively."

W. ZENTMAYER.

Physiology

THE MECHANISM OF AQUEOUS SECRETION IN MAMMALIA. T. HENDERSON, Brit. J. Ophth. 25:30 (Jan.) 1941.

In conclusion Henderson says:

"A study of the comparative anatomy of the angle of the anterior chamber in mammalia demonstrates the following:—

"(1) The anatomical conditions in the eye negative aqueous formation by mere physical operations.

"(2) The first insurmountable obstacle to the theory of aqueous formation by dialysis or filtration or any combination of the two, is the fact that the stroma of the ciliary body and processes is in free communication with the aqueous at the angle.

"(3) The second and equally insuperable objection is the presence of the double layer of epithelial cells covering the ciliary processes and lining the back of the iris.

"(4) The aqueous cannot be a dialysis from the capillaries of the ciliary processes because such a fluid will still be on the wrong side of the ciliary epithelium, only to drain directly into the angle.

"(5) The aqueous cannot be a filtration as there is no difference of hydrostatic level between the two sides of the ciliary epithelium.

"(6) The aqueous cannot be a filtrate-dialysis as the components of the combination are mechanically ineffective.

"From the clinical aspect, the condition of iris bombé and its relief by iridectomy are practical proof that the epithelium covering the processes

and back of the iris is not an inert membrane. Only by secretory activity can fluid be transmitted from the capillaries of the ciliary processes into the posterior chamber and iris bombé results because pigmented iris epithelium is not porous. Filtrate dialysis is a conception of function operating without a mechanism."

The article is illustrated.

W. ZENTMAYER.

Refraction and Accommodation

NEW THOUGHTS ON THE ORIGIN OF MYOPIA. K. LINDNER, *Klin. Monatsbl. f. Augenh.* 103:582 (Dec.) 1939.

Lindner contradicts Steiger's idea that the myopia of school children is an unavoidable hereditary destiny, maintaining that its progress may be stopped by exact correction of the visual error, limitation of close work and other precautionary measures. He goes as far as to say that the development of myopia may be prevented in most cases by elimination of near work and that malignant myopia may be arrested by proper measures. That heredity cannot be an essential factor in the causation of the myopia of school children may be gathered from the fact that this type of myopia was more frequent in catholic students of theology, whose parents were farmers or working people, than among protestant students of theology, who were descendants of teachers or preachers. It is caused by near work. Heredity, on the other hand, is an essential factor in malignant myopia, which may occur without the influence of close work. Lindner blames disturbances of the capillaries by toxins and a deficiency of oxygen for the thinning of the sclera. Blood plasma and enzymes accumulate because of the toxic lesion or the oxygen deficiency in a quantity which cannot be handled by the venous capillaries and by the vortex veins. With normal intraocular pressure extension of the sclera may follow gradually as a result of softening of the sclera by the abnormal composition of the nourishing fluid, which contains, for example, an excess of carbon dioxide. Unilateral myopia may be explained by abnormal narrowing of the vortex veins or insufficient development of the subcapillary and suprachoroidal membranes of one eye.

Myopia may develop during or as a consequence of severe general diseases through damage to the capillaries and serous permeation of the choroid in the area of the posterior pole of the eye which receives the greater strain.

Only that type of near work will increase myopia which demands extensive metabolism of the retina, namely reading, with its constant change of the picture under observation. Watch makers show little tendency toward myopia because they observe more or less the same picture during their work. Type setters, on the other hand, show a high percentage of myopia because, although their work is not especially close to the eyes, they are constantly under the influence of poisons which lead to lesions of the capillaries and an increase in the transudation of plasma and enzymes, with their damaging influence on the sclera.

K. L. STOLL.

STABILITY OF ACCOMMODATION IN PATIENTS WITH INFECTIOUS DISEASES. B. KALASHNIKOFF, *Vestnik oftal.* 14:35, 1939.

An ergograph constructed by Zimkin in 1932 and the method of using it are described. Kalashnikoff made 414 examinations of patients with infectious diseases and of persons with normal eyes, using atropine given by mouth and by rectum; 1,014 examinations (2,850 curves) with various objects made it possible to establish five types of curves of stability of accommodation (illustrated). Study of the curves associated with tonsillitis, grip, pneumonia, typhoid and malaria showed an absence of specificity. The type of the curve depends mostly on the state of toxicity of the accommodative apparatus during the examination and the illness, as any type of curve might be obtained, from the fifth to the first individually or in various combinations. A detailed analysis of the curves is given. Kalashnikoff arrives at the following conclusions:

1. The influence of infection on the accommodative apparatus varies. The oculomotor nerve endings are affected; in some cases the whole ciliary body and in others the nuclei of the oculomotor nerve are involved. Other factors as well as the direct influence of the affected accommodative apparatus influence the appearance of the ergograms of patients with infectious diseases. Spacing between the shaded lines occurs in the ergograms of patients with high temperatures because, owing to their difficulty in concentration due to weakness, the handle is not moved fast enough.

2. None of the aforementioned diseases have a specific action on the accommodative apparatus; the chief thing is the intoxication of the accommodative apparatus, which can be slight, moderate or severe. Since various pathologic changes go on in the organism, there are combined forms of weakening of the accommodative apparatus as a whole, with no relation to the character of the disease as a nosologic unit.

3. Tonsillitis and grip weaken the accommodation most severely; sometimes the weakness lasts for a month, i. e. longer than the convalescence. After pneumonia and typhoid the accommodation returns to normal during the convalescent period.

4. The ergograph should be used more frequently for examination of the stability of accommodation of patients with infectious diseases. Close work should not be allowed too soon after the illness. During the period of convalescence the illumination and the position of the patient should be adjusted according to the patient's requirements.

O. SITCHEVSKA.

Retina and Optic Nerve

THE DYSTROPHIES OF THE MACULA. A. SORSBY, *Brit. J. Ophth.* 24: 469 (Oct.) 1940.

Sorsby briefly reviews the different varieties of familial diseases confined largely or exclusively to the central area of the fundus and draws the following conclusions:

"Macular dystrophy presents such a protean range of manifestations that the classification suggested by Behr, helpful as it has been, must be

regarded as distinctly schematic. The range of ophthalmoscopic appearances extends from faint mottling of the macular zone to the picture seen in 'Doyne's choroiditis,' almost every possible intermediate lesion having been reported. The conception of a distinctly isolated macular lesion is not valid. There may be present, not only extensive perimacular involvement but also peripheral lesions, and some general involvement of the whole fundus is not excessively rare. One case is reported showing the association of macular dystrophy with typical retinitis pigmentosa. A rigid classification of the macular dystrophies on a chronological basis involving distinct age-groups, as postulated by Behr, is not borne out by experience. The age of incidence extends, just as the ophthalmoscopic appearances do, over a continuous unbroken range.

"The apparent complexity of abiotrophic central lesions of the fundus lends itself to considerable simplification. Three clear cut types are recognizable.

"(1) Central choroidal sclerosis as shown in a previous paper. Here the primary lesion develops in the vascular bed of the choroid.

"(2) Angeoid streaks—which must now be regarded as part of the generalized process of elastosis dystrophica—produced by ruptures in the membrane of Bruch and followed by secondary changes.

"(3) Central retinal dystrophy: Theoretically the central retinal dystrophies might show several sub-varieties; two neuro-epithelial types, in one the rods would be involved, in the other the cones; a type dependent upon degeneration of the ganglion cells; and a further type dependent upon changes in the retinal capillaries supplying the central area. On the present material and almost total lack of histological information, this fine subdivision is impossible."

Sorsby presents the following summary of his article:

"(1) Eight familial groups of macular dystrophy are reported.

"(2) They illustrate the great range of ophthalmoscopic appearances, extending from fine mottling of the maculae to 'exudative' reactions, 'inverse retinitis pigmentosa,' intense central pigmentary changes, hole formation, extensive perimacular involvement and the patterned reaction of 'Doyne's choroiditis.'

"(3) Symptomatically macular dystrophy has an equally wide range. The symptoms may be so severe as to constitute total day blindness (total colour blindness) or so mild that vision is hardly affected. The condition is not necessarily rapid and relentlessly progressive.

"(4) On the basis of these cases, supported by an analysis of the material recorded in the literature, it is held that Best's congenital macular degeneration, Doyne's choroiditis, Stargardt's disease and the numerous types of central macular dystrophy described by different observers constitute a single clinical entity with more than one mode of inheritance.

"(5) This central retinal dystrophy has to be distinguished from central choroidal dystrophy (central choroidal sclerosis) and central internal limiting membrane dystrophy (angeoid streaks)."

The article is illustrated with more than fifty black and white drawings and a number of colored plates.

In an appendix to Sorsby's article Hans Grüneberg adds a note on the genetic aspects of the macular dystrophies. He says: ". . . no decision is yet possible. There undoubtedly exists families in which the lesions are (more or less irregularly) dominant, and there undoubtedly are families where the anomaly is due to a recessive gene (or genes), as evidenced by the high incidence of consanguineous marriages. This difference alone does not prove that the group is genetically heterogeneous, as dominant and recessive types may belong to the same allelomorphic series. On the other hand, there is no genetic proof that the group is homogeneous. The issue cannot be decided on the incomplete genetic evidence available as yet."

W. ZENTMAYER.

Uvea

CHORIORETINITIS CENTRALIS SEROSA DIFFERENTIATED FROM RETINITIS CENTRALIS ANGIONEUROTICA. E. B. STREIFF, *Klin. Monatsbl. f. Augenh.* 103:524 (Oct.-Nov.) 1939.

Chorioretinitis centralis serosa was first described by Asayama in 1897 and then by other Japanese authors. This disease, apparently frequent in Japan, is very rare in Europe. The patients, mostly men, complain of microtelepsy, metamorphosis, central scotoma, more often relative than absolute, disturbed color perception and some other symptoms. The vision is usually undisturbed. The retina in the macular region shows well defined edema surrounded by a reflex ring. Fine grayish white dots occur within the edematous areas at a later stage. Complicating symptoms of tuberculosis, of focal infection and, rarely, of syphilis were observed. Streiff reports 2 cases, that of a woman aged 21 and that of a man aged 27. The details of the first case tally with the Japanese reports. In the second case additional symptoms were noted—a formation in the lower portion of the bullous macular edema, resembling a hypopyon; long duration of the disease, and unfavorable prognosis for the vision. Comparison of the symptoms of chorioretinitis centralis serosa and of retinitis centralis angioneurotica shows the difference between these two diseases.

K. L. STOLL.

Society Transactions

EDITED BY DR. W. L. BENEDICT

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ALGERNON REESE, M.D., *Chairman*

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March 17, 1941

SYMPOSIUM ON TUMORS OF THE EYE AND ITS ADNEXA

Tumors of the Eyeball. DR. THEODORE L. TERRY (by invitation), Boston.

More than two fifths of retroiridial malignant melanomas are not suspected at the time of enucleation. The tumor may be hidden by unilateral glaucoma or uveitis and in many cases has been mistaken for a simple separation of the retina.

Conditions simulating the malignant melanoma are disciform degeneration, angioma, neurofibroma, meningioma, dykthoma, metastatic chorionepithelioma and carcinoma. A retinoblastoma filling the globe must be differentiated from a persistent tunica vasculosa lentis.

Tumors of the Orbit. DR. C. S. O'BRIEN (by invitation), Iowa City.

The orbital tumor occurs at all ages. It may be benign or malignant, primary or secondary. A secondary tumor may be the result of extension or of metastasis. It usually produces exophthalmos, displacement of the globe and limitation of ocular movements. There may be other symptoms and signs, such as a visible or palpable mass in the orbit, diplopia, edema of the lids, chemosis, hemorrhages, atrophy of the optic nerve and papilledema. Tumor-like lesions, such as inflammatory pseudotumor, mucocoele, cyst, hematoma, emphysema and pulsating exophthalmos, must be differentiated. Often roentgenograms are an aid to diagnosis. As a rule one cannot determine the type of tumor without a biopsy. The treatment varies. Excision of the tumor may be indicated, exenteration of the orbit may be necessary, irradiation may be the treatment of choice or other measures may be tried.

Tumors of Conjunctiva and Lids: A Brief Review. DR. BERNARD SAMUELS.

This article is published in full in this issue of the ARCHIVES, page 789.

DISCUSSION OF PAPERS IN SYMPOSIUM

DR. JAMES EWING (by invitation): I think I speak for the audience as well as for myself in expressing great satisfaction in being able in

one evening to obtain from authorities in different parts of the country such an extensive and intensive postgraduate course on tumors of the eye. It is to the credit of ophthalmologists that in their specialty clinicians have taken over very competently the field of pathology. I do not know that the same accomplishment has been attained in any other medical specialty. Nevertheless, general pathologists, particularly those who specialize in the pathology of tumors, have a great interest in tumors of the eye, although under ordinary circumstances it is almost impossible for them to obtain enough material to compete with ophthalmologists in this broad subject.

I was impressed by two features of Dr. O'Brien's presentation: First, he has described as occurring in the eye almost every type of tumor which develops in the body; second, he was thoroughly impressive in speaking of the necessity for the ophthalmopathologist to be proficient in general pathology and in clinical diagnosis as well so as to be able to recognize the primary source of the disease when examining a patient with a tumor of the eye. The failure to recognize the primary source of the disease is in my opinion the chief fault in the treatment of malignant tumors in general. Some physicians do not make a thorough examination of the patient; they see the tumor and treat it, and the patient suffers the consequences. Finally, Dr. O'Brien's paper was so comprehensive and exhaustive that it reminded me of the fact that one of the bulkiest volumes which covers any one group of tumors refers to the eye, Félix Lagrange's "*Les tumeurs de l'oeil, de l'orbite et des annexes*" (Paris, G. Steinheil, 1901).

I should like to make some inquiries relating to Dr. Terry's discussion of melanomas of the eye. The problem of melanomas is more acute in relation to the eye than to any other part of the body. From the book entitled "*Debatable Tumors in Human and Animal Pathology*," I was surprised to learn that the authors, Dawson, Innes and Harvey, of Edinburgh, concluded that certain ocular melanomas originate from the pigmented cells of the retina. They reached this opinion after research in the field of embryology. I did not know that there was a type of melanoma oculi derived from such cells.

Not long ago I examined an eye which had been removed because of a small tumor in the anterior portion, near the lens, which I regarded as a benign nevus. My question pertaining to the ophthalmologist's recognizing a benign nevus in an eye, in which case enucleation of the entire eye is not necessary, has been answered by Dr. Terry. How often an eye has been enucleated because of a benign nevus no one knows. However, the facts that benign nevi occur in the eye as they do in the skin and that a benign nevus in the eye does not require enucleation are worth emphasizing.

I should like to know the prevailing opinion regarding the exact origin of the choroidal melanoma. Does it arise from the chromatophores of the choroid or from isolated groups of cells of the type of nevi? I have never been able to form an opinion because I have never seen a melanoma of the choroid in its early formation. Fuchs, Parsons and other investigators have observed such nevi in the choroid and considered them as probably originating from melanomas. I should appreciate it if Dr. Terry would discuss this phase.

I should like to know whether a traumatic melanoma has ever been observed. I have recently gone over the literature on this subject, and I am not convinced that it has. I do not believe that a case of a traumatic melanoma which would satisfy a critical observer has ever been reported. I believe that repeated trauma will produce a melanoma in previously normal tissue; for instance, trauma produced by stepping on a nail in the sole of a shoe may cause a tumor in a previously normal foot. I do not know whether traumatic melanomas occur in the eye, but Dr. Verhoeff and Dr. Knapp told me recently that they had never seen a traumatic melanoma of the eye.

I am happy to be able to describe a tumor of the eye which has not been referred to by any of the speakers here. I am indebted to Dr. Kelly, of St. Vincent's Hospital, for this opportunity. This tumor developed in 2 of his younger patients. It filled the orbit, caused the eyeball to protrude, was attached to the orbital periosteum and extended back to the apex. In each case, although the tumor was only partially removed it did not fungate like a malignant melanoma. It was coal black and hard, like a neurofibroma. It was composed of adult chromatophores. In 1 case there was a white streak about 4 mm. in diameter through the center of the tumor and on section this proved to be a neuroma or a neurinoma. How would these two tumors be classified? Apparently they were not malignant, because they have not recurred. Possibly they will recur later. They certainly did not have the characteristics of malignant melanomas. My conclusion is that they were tumors of a peculiar type, which could best be called the chromatophoroma. They were comparable to the mongolian spot, which is a benign process composed exclusively of adult chromatophores. Relatively benign chromatophoromas also occur in the epidermis.

I am of the opinion that melanomas should not all be classified as of one type. According to Masson, there is one type which is derived from the specialized cells of the peripheral sensory nerve endings. It is malignant. There is another type composed of chromatophores, which I prefer to call chromatophoromas, which is illustrated in the 2 cases of an intraorbital melanoma which I have just described. There is also evidence in favor of classifying the comparatively benign chromatophoroma with melanosis oculi, although diffuse melanosis usually terminates fatally. Finally, the mongolian spot is a chronic, comparatively benign tumor composed exclusively of chromatophores. I am inclined to think that ophthalmologists should entertain the idea of recognizing in and about the eye a benign type of chromatophoroma, separate from true melanoma.

DR. LOUISE H. MEEKER: The little I have to offer can best be illustrated by showing three pictures on the screen. (Slides were shown.)

CASE 1 (Hemangioma of the Choroid).—In more than twenty-five years but one tumor of this kind has been examined in the laboratory with which I am associated. The eye was removed because of absolute glaucoma and because of intense pain which had continued for two weeks. The patient had been growing blind for ten years. When the eye was sectioned the folds of the retina were seen to hide the tumor, which was at the right of the papilla. The tumor was not disclosed

until sections were made for microscopic study. In the next slide, of higher magnification, it is evident that a cavernous hemangioma (a benign tumor) was present. No other nevus was observed.

CASE 2 (Amputation Neuroma).—The tumor in this case also was not suspected when the eye was enucleated. The patient was a youth 19 years old who had been blind since birth. He had a "phthisis bulbi" eye. At the left was a loop of the long posterior ciliary nerve under the conjunctiva. On the right the long posterior ciliary nerve, together with tissues of the eye, was ruptured by the instrumental delivery. The nerve could be seen to have grown through the choroid and was enlarged greatly at the ciliary body. (The darker blue areas are calcific deposits.) In the square are groups of ganglion cells, which could be seen at various points over the nerve. The tumor was benign, and there had been no recurrence at the end of five years.

CASE 3 (Plexiform Neuroma of the Choroid).—In this case diagnosis of absolute glaucoma, ulcer of the cornea and hypopyon were made after removal of the eye. Glaucoma was evidenced by the appearance of the narrowed angles, the adherent iris and the cupped disk. At the fundus the choroid was thickened and extended from the equator. Much of the stroma of the choroid was replaced by nerve fibers, which extended about the large vessel and through the sclera. Many ganglion cells were scattered over the nerve trunks. There were twenty-nine such cells in a single section. In this instance also, at the end of five years there had been no recurrence.

DR. THEODORE L. TERRY: Of course it is always a real treat to hear Dr. Ewing.

Perhaps the huge variety of neoplasms to be found in the eye may be directly related to the complexity of the embryonic development of the eye. The mingling and mixing of various embryonic tissues, such as surface ectoderm, neural ectoderm and mesoderm, with the formation of tissue so different from that usually produced by such embryonic layers, may well give opportunity for tumors to arise. Although many pathologic lesions in the choroid give rise to production of bone, I have not seen a bone tumor of the choroid, but if I interpret Dr. Ewing's nod correctly, and I see by his smile that I do, he has seen even that. The questions Dr. Ewing brought up are difficult or impossible to answer explicitly. His further discussion has presented to my mind perhaps as good an answer as can be given. It is my feeling also that a melanoma of the choroid cannot arise from the pigment epithelium of the retina because Bruch's membrane is formed so early. However, tissue continuous with and similar to the pigment epithelium of the retina may take part in the production of the so-called adenoma of the ciliary body and also may have something to do with the neoplasm called dykthoma by some observers. Certainly, eyes have been removed because of a neoplasm which turned out to be a benign melanoma, or should one say a nevus? In my original discussion I intended to point out the method of distinguishing between an angioma and a melanoma by compression of the globe. Under pressure an angioma should partially collapse, but the value of pressure in such a differentiation has not been proved so far as I know. After observing a true leiomyosarcoma of the lid become a round cell sarcoma under repeated, unsuc-

cessful attempts at removal, I thought that perhaps this process might be a key to the origin of the intraocular malignant melanoma, since the pigment of the smooth muscle is a part of the uvea, but further consideration makes this theory seem overdrawn. It is my opinion that such a tumor may arise from cells which ordinarily produce or mature into chromatophores. The suggestion of Masson concerning the origin of cells bearing melanin is interesting. Theobald applied this view to the origin of the malignant melanoma of the choroid, but her arguments were based on relatively large neoplasms. I think this contention can be proved only by extremely small tumors, because any neoplasm of the choroid that approximates 1 cm. in diameter would necessarily contact nerves somewhere.

It is interesting to hear what Dr. Ewing offered concerning the two possible types of tumors.

The possibility that trauma is an important etiologic factor always is interesting. The frequency of trauma to the eye is so great that its relation to the origin of melanomas is questionable. It is not extremely uncommon for a person with an intraocular foreign body not to know when it could have entered the eye. One can have trauma to the eye, then, without remembering it. At present, I rather feel that trauma as an etiologic factor is of questionable importance.

The term chromatophoroma seems a good one.

The illustrations shown by Dr. Meeker elaborated the subject under discussion in a most interesting manner.

Directory of Ophthalmologic Societies *

INTERNATIONAL

INTERNATIONAL ASSOCIATION FOR PREVENTION OF BLINDNESS

President: Dr. P. Baillart, 66 Boulevard Saint-Michel, Paris, 6^e, France.

Secretary-General: Prof. M. Van Duyse, Université de Gand, Gand, Prov. Ostflandern, Belgium.

All correspondence should be addressed to the Secretariat, 66 Boulevard Saint-Michel, Paris, 6^e, France.

INTERNATIONAL OPHTHALMOLOGIC CONGRESS

President: Prof. Nordenson, Serafimerlasarettet, Stockholm, Sweden.

Secretary: Dr. Ehlers, Jerbanenegade 41, Copenhagen, Denmark.

INTERNATIONAL ORGANIZATION AGAINST TRACHOMA

President: Dr. A. F. MacCallan, 17 Horseferry Rd., London, England.

PAN-AMERICAN CONGRESS OF OPHTHALMOLOGY

President: Dr. Harry S. Gradle, 58 E. Washington St., Chicago.

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FOREIGN

ALL-INDIA OPHTHALMOLOGICAL SOCIETY

President: Dr. B. K. Narayan Rao, Minto Ophthalmic Hospital, Bangalore.

Secretary: Dr. G. Zachariah, Flitcham, Marshall's Rd., Madras.

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Secretary: Dr. Frederick Ridley, 12 Wimpole St., London, W. 1.

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Secretary: Dr. F. S. Tsang, 221 Foochow Rd., Shanghai.

CHINESE OPHTHALMOLOGICAL SOCIETY OF PEIPING

President: Dr. H. T. Pi, Peiping Union Medical College, Peiping.

Secretary: Dr. C. K. Lin, 180 Hsi-Lo-yen, Chienmeng, Peiping.

Place: Peiping Union Medical College, Peiping. Time: Last Friday of each month.

GERMAN OPHTHALMOLOGICAL SOCIETY

President: Prof. W. Lohlein, Berlin.

Secretary: Prof. E. Engelking, Heidelberg.

HUNGARIAN OPHTHALMOLOGICAL SOCIETY

President: Prof. H. G. Ditroi, Szeged.

Assistant Secretary: Dr. Stephen de Grosz, University Eye Hospital, Maria ucca 39, Budapest.

All correspondence should be addressed to the Assistant Secretary.

MIDLAND OPHTHALMOLOGICAL SOCIETY

President: Dr. W. Niccol, 4 College Green, Gloucester, England.

Secretary: Mr. T. Harrison Butler, 61 Newhall St., Birmingham 3, England.

Place: Birmingham and Midland Eye Hospital.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and keep it up to date.

NORTH OF ENGLAND OPHTHALMOLOGICAL SOCIETY

President: Dr. A. MacRae, 6 Jesmond Rd., Newcastle-upon-Tyne, England.
 Secretary: Dr. Percival J. Hay, 350 Glossop Rd., Sheffield 10, England.
 Place: Manchester, Bradford, Leeds, Newcastle-upon-Tyne, Liverpool and Sheffield, in rotation. Time: October to April.

OPHTHALMOLOGICAL SOCIETY OF AUSTRALIA

President: Dr. A. James Flynn, 135 Macquarie St., Sydney.
 Secretary: Dr. D. Williams, 193 Macquarie St., Sydney.

OPHTHALMOLOGICAL SOCIETY OF EGYPT

President: Prof. Dr. Mohammed Mahfouz Bey, Government Hospital, Alexandria.
 Secretary: Dr. Mohammed Khalil, 4 Baehler St., Cairo.
 All correspondence should be addressed to the Secretary, Dr. Mohammed Khalil.

OPHTHALMOLOGICAL SOCIETY OF THE UNITED KINGDOM

President: Mr. T. Harrison Butler, 61 Newhall St., Birmingham 3, England.
 Secretary: Mr. L. H. Savin, 7 Queen St., London, W. 1, England.

OPHTHALMOLOGY SOCIETY OF BOMBAY

President: Dr. D. D. Sathaye, 127 Girgaum Rd., Bombay 4, India.
 Secretary: Dr. H. D. Dastur, Dadar, Bombay 14, India.
 Place: H. B. A. Free Ophthalmic Hospital, Parel, Bombay 12. Time: First Friday of every month.

OXFORD OPHTHALMOLOGICAL CONGRESS

Master: Dr. Percival J. Hay, 350 Glossop Rd., Sheffield 10, England.
 Secretary-Treasurer: Dr. F. A. Anderson, 12 St. John's Hill, Shrewsbury, England.

PALESTINE OPHTHALMOLOGICAL SOCIETY

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 Secretary: Dr. E. Sinai, Tel Aviv.

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 Secretary: Dr. J. Sobański, Lindley'a 4, Warsaw.
 Place: Lindley'a 4, Warsaw.

ROYAL SOCIETY OF MEDICINE, SECTION OF OPHTHALMOLOGY

President: Dr. A. J. Ballantyne, 11 Sandyford Pl., Glasgow, C. 3, Scotland.
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SOCIEDAD OFTALMOLOGIA DEL LITORAL, ROSARIO (ARGENTINA)

President: Prof. Dr. Carlos Weskamp, Laprida 1159, Rosario.
 Secretary: Dr. Juan M. Vila Ortiz, Córdoba 1433, Rosario.
 Place: Rosario. Time: Last Saturday of every month, April to November, inclusive.
 All correspondence should be addressed to the President.

SOCIEDADE DE OPHTALMOLOGIA E OTO-RHINO-LARYNGOLOGIA DA BAHIA

President: Dr. Francisco Ferreira, Pitangueiras 15, Brotas, S. Salvador, Brazil.
 Secretary: Dr. Adroaldo de Alencar, Brazil.
 All correspondence should be addressed to the President.

SOCIETÀ OFTALMOLOGICA ITALIANA

President: Prof. Dott. Giuseppe Ovio, Ophthalmological Clinic, University of Rome, Rome.
 Secretary: Prof. Dott. Epimaco Leonardi, Via del Gianicolo, 1, Rome.

SOCIÉTÉ FRANÇAISE D'OPHTALMOLOGIE

Secretary: Dr. René Onfray, 6 Avenue de la Motte Picquet, Paris, 7^e.

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Secretary: Dr. Sadger Max, 9 Bialik St., Tel Aviv, Palestine.

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON OPHTHALMOLOGY

Chairman: Dr. Lawrence T. Post, 508 N. Grand Blvd., St. Louis, Mo.

Secretary: Dr. Derrick Vail, 441 Vine St., Cincinnati.

Place: Atlantic City. Time: June 8-12, 1942.

AMERICAN ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY, SECTION ON OPHTHALMOLOGY

President: Dr. Frank R. Spencer, Physicians' Bldg., Boulder, Colo.

President-Elect: Dr. Ralph I. Lloyd, 14-8th Ave., Brooklyn.

Executive Secretary-Treasurer: Dr. William P. Wherry, 1500 Medical Arts Bldg., Omaha.

Place: Chicago. Time: Oct. 19-24, 1941.

AMERICAN OPHTHALMOLOGICAL SOCIETY

President: Dr. Allen Greenwood, 82 Commonwealth Ave., Boston.

Secretary-Treasurer: Dr. Eugene M. Blake, 303 Whitney Ave., New Haven, Conn.

ASSOCIATION FOR RESEARCH IN OPHTHALMOLOGY, INC.

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CANADIAN MEDICAL ASSOCIATION, SECTION ON OPHTHALMOLOGY

President: Dr. Alexander E. MacDonald, 170 St. George St., Toronto.

Secretary-Treasurer: Dr. L. J. Sebert, 170 St. George St., Toronto.

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Secretary-Treasurer: Dr. Alexander E. MacDonald, 421 Medical Arts Bldg., Toronto.

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Executive Director: Mrs. Eleanor Brown Merrill, 1790 Broadway, New York.

SECTIONAL

ACADEMY OF MEDICINE OF NORTHERN NEW JERSEY, SECTION ON EYE, EAR, NOSE AND THROAT

President: Dr. Charles W. Barkhorn, 223 Roseville Ave., Newark.

Secretary: Dr. William F. McKim, 317 Roseville Ave., Newark.

Place: 91 Lincoln Park South, Newark. Time: 8:45 p. m., second Monday of each month, October to May.

CENTRAL WISCONSIN SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. J. V. May, 1703 Main St., Marinette.

Secretary: Dr. G. L. McCormick, 626 S. Central Ave., Marshfield.

Place: Marinette. Time: November 1941.

NEW ENGLAND OPHTHALMOLOGICAL SOCIETY

President: Dr. William D. Rowland, 84 Commonwealth Ave., Boston.
 Secretary-Treasurer: Dr. Trygve Gundersen, 243 Charles St., Boston.
 Place: Massachusetts Eye and Ear Infirmary, 243 Charles St., Boston. Time:
 8 p. m., third Tuesday of each month from November to April, inclusive.

PACIFIC COAST OTO-OPHTHALMOLOGICAL SOCIETY

President: Dr. Isaac H. Jones, 635 S. Westlake Ave., Los Angeles.
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 Secretary-Treasurer: Dr. Barton E. Peden, 419 Stimson Bldg., Seattle.
 Place: Seattle or Tacoma, Wash. Time: Third Tuesday of each month, except
 June, July and August.

ROCK RIVER VALLEY EYE, EAR, NOSE AND THROAT SOCIETY

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 Secretary-Treasurer: Dr. Harry R. Warner, 321 W. State St., Rockford, Ill.
 Place: Rockford, Ill., or Janesville or Beloit, Wis. Time: Third Tuesday of
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SAGINAW VALLEY ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. M. Kessler, 311 Center Ave., Bay City, Mich.
 Secretary-Treasurer: Dr. J. H. Curts, 330 S. Washington Ave., Saginaw, Mich.
 Place: Saginaw or Bay City, Mich. Time: Second Tuesday of each month, except
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SIoux VALLEY EYE AND EAR ACADEMY

President: Dr. J. C. Davis, 1615 Howard St., Omaha.
 Secretary-Treasurer: Dr. J. E. Dvorak, 408 Davidson Bldg., Sioux Falls, S. D.

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SOUTHWESTERN MICHIGAN TRIOLOGICAL SOCIETY

President: Dr. W. M. Dodge, 716 First National Bank Bldg., Battle Creek.
 Secretary-Treasurer: Dr. Kenneth Lowe, 25 W. Michigan Ave., Battle Creek.
 Time: Last Thursday of September, October, November, March, April and May.

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President: Dr. C. H. Bailey, 29 S. Oakland Ave., Sharon.
 Secretary-Treasurer: Dr. J. McClure Tyson, Deposit Nat'l Bank Bldg., DuBois.

STATE

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 Secretary-Treasurer: Dr. Raymond C. Cook, 701 Main St., Little Rock.

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President: Dr. William M. Bane, 1612 Tremont Pl., Denver.
 Secretary: Dr. Harry Shankel, Republic Bldg., Denver.
 Place: University Club, Denver. Time: 7:30 p. m., third Saturday of each
 month, October to May, inclusive.

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NOSE AND THROAT

President: Dr. Edward N. DeWitt, 836 Myrtle Ave., Bridgeport.
Secretary-Treasurer: Dr. Henry L. Birge, 179 Allyn St., Hartford.

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President: Dr. E. N. Maner, 247 Bull St., Savannah.
Secretary-Treasurer: Dr. C. K. McLaughlin, 567 Walnut St., Macon.

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President: Dr. F. McK. Ruby, Union City.
Secretary: Dr. Edwin W. Dyar Jr., 23 E. Ohio St., Indianapolis.
Place: French Lick. Time: First Wednesday in April.

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President: Dr. J. K. Von Lackum, 117-3d St. S.E., Cedar Rapids.
Secretary-Treasurer: Dr. B. M. Merkel, 604 Locust St., Des Moines.

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Secretary-Treasurer: Dr. Edley H. Jones, 1301 Washington St., Vicksburg, Miss.

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AND OTOLARYNGOLOGY

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Secretary: Dr. R. G. Laird, 114 Fulton St., Grand Rapids.

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Secretary-Treasurer: Dr. George E. McGeary, 920 Medical Arts Bldg., Minneapolis.
Time: Second Friday of each month from October to May.

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President: Dr. A. L. Hammerel, 208 N. Broadway, Billings.
Secretary: Dr. Fritz D. Hurd, 309 Medical Arts Bldg., Great Falls.

NEBRASKA ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. John Peterson, 1307 N St., Lincoln.

NEW JERSEY STATE MEDICAL SOCIETY, SECTION ON OPHTHALMOLOGY,
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Secretary: Dr. Arthur E. Sherman, 243 S. Harrison St., East Orange.

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Secretary: Dr. C. Stewart Nash, 277 Alexander St., Rochester.

NORTH CAROLINA EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. M. R. Gibson, Professional Bldg., Raleigh.
Secretary: Dr. Vanderbilt F. Couch, 105 W. 4th St., Winston-Salem.

NORTH DAKOTA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. A. E. Spear, Dickinson.
Secretary-Treasurer: Dr. F. L. Wicks, 516-6th St., Valley City.

OREGON ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Paul Bailey, 833 S. W. 11th Ave., Portland.
 Secretary-Treasurer: Dr. R. S. Fixott, 1020 S. W. Taylor St., Portland.
 Place: Good Samaritan Hospital, Portland. Time: Third Tuesday of each month.

RHODE ISLAND OPHTHALMOLOGICAL AND OTOLOGICAL SOCIETY

Acting President: Dr. N. Darrell Harvey, 112 Waterman St., Providence.
 Secretary-Treasurer: Dr. Linley C. Happ, 124 Waterman St., Providence.
 Place: Rhode Island Medical Society Library, Providence. Time: 8:30 p. m.,
 second Thursday in October, December, February and April.

SOUTH CAROLINA SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. Roderick Macdonald, Rock Hill.
 Secretary: Dr. J. W. Jervy Jr., 101 Church St., Greenville.
 Place: Columbia Hotel, Columbia. Time: November 1941.

TENNESSEE ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. Wesley Wilkerson, 700 Church St., Nashville.
 Secretary-Treasurer: Dr. W. D. Stinson, 124 Physicians and Surgeons Bldg.,
 Memphis.

TEXAS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President: Dr. E. L. Goar, 1300 Walker Ave., Houston.
 Secretary: Dr. Dan Brannin, 929 Medical Arts Bldg., Dallas.
 Place: San Antonio. Time: December 1941.

UTAH OPHTHALMOLOGICAL SOCIETY

President: Dr. Everett B. Muir, Boston Bldg., Salt Lake City.
 Secretary-Treasurer: Dr. Earl H. Phillips, 623 Judge Bldg., Salt Lake City.
 Place: University Club, Salt Lake City. Time: 7:00 p. m., third Monday of
 each month.

VIRGINIA SOCIETY OF OTO-LARYNGOLOGY AND OPHTHALMOLOGY

President: Dr. George G. Hawkins, Newport News.
 Secretary-Treasurer: Dr. Guy Fisher, 3 E. Beverley St., Staunton.

WEST VIRGINIA STATE MEDICAL ASSOCIATION, EYE, EAR, NOSE
 AND THROAT SECTION

President: Dr. George Traugh, 309 Cleveland Ave., Fairmont.
 Secretary: Dr. Welch England, 621½ Market St., Parkersburg.

LOCAL

AKRON ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. George E. Black, 7 W. Bowery St., Akron, Ohio.
 Secretary-Treasurer: Dr. C. R. Andersen, 106 S. Main St., Akron, Ohio.
 Time: First Monday in January, March, May and November.

ATLANTA EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. Stacy C. Howell, 144 Ponce de Leon Ave. N. E., Atlanta, Ga.
 Secretary: Dr. Lester A. Brown, 478 Peachtree St. N. E., Atlanta, Ga.
 Place: Grady Hospital. Time: 6:00 p. m., second Wednesday of each month
 from October to May.

BALTIMORE MEDICAL SOCIETY, SECTION ON OPHTHALMOLOGY

Chairman: Dr. Ernst Bodenheimer, 1212 Eutaw Pl., Baltimore.
 Secretary: Dr. Thomas R. O'Rourke, 104 W. Madison St., Baltimore.
 Place: Medical and Chirurgical Faculty, 1211 Cathedral St. Time: 8:30 p. m.
 fourth Thursday of each month from October to March.

BIRMINGHAM EYE, EAR, NOSE AND THROAT CLUB

President: Each member, in alphabetical order.

Secretary: Dr. Luther E. Wilson, 919 Woodward Bldg., Birmingham, Ala.

Place: Tutwiler Hotel. Time: 6:30 p. m., second Tuesday of each month, September to May, inclusive.

BROOKLYN OPHTHALMOLOGICAL SOCIETY

President: Dr. Maurice Wieselthier, 1322 Union St., Brooklyn.

Secretary-Treasurer: Dr. Harold F. Schilback, 142 Joralemon St., Brooklyn.

Place: Kings County Medical Society Bldg., 1313 Bedford Ave. Time: Third Thursday in February, April, May, October and December.

BUFFALO OPHTHALMOLOGIC CLUB

President: Dr. Meyer H. Riweh, 367 Linwood Ave., Buffalo.

Secretary-Treasurer: Dr. Sheldon B. Freeman, 196 Linwood Ave., Buffalo.

Time: Second Thursday of each month.

CHATTANOOGA SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Each member, in alphabetical order.

Secretary: Dr. Douglas Chamberlain, Chattanooga Bank Bldg., Chattanooga, Tenn.

Place: Mountain City Club. Time: Second Thursday of each month from September to May.

CHICAGO OPHTHALMOLOGICAL SOCIETY

President: Dr. Sanford Gifford, 720 N. Michigan Ave., Chicago.

Secretary-Treasurer: Dr. Vernon M. Leech, 55 E. Washington St., Chicago.

Place: Chicago Towers Club, 505 N. Michigan Ave. Time: Third Monday of each month from October to May.

CINCINNATI GENERAL HOSPITAL OPHTHALMOLOGY STAFF

Chairman: Dr. D. T. Vail, 441 Vine St., Cincinnati.

Secretary: Dr. A. A. Levin, 441 Vine St., Cincinnati.

Place: Cincinnati General Hospital. Time: 7:45 p. m., third Friday of each month except June, July and August.

CLEVELAND OPHTHALMOLOGICAL CLUB

Chairman: Dr. W. J. Abbott, 10515 Carnegie Ave., Cleveland.

Secretary: Dr. L. V. Johnson, 2065 Adelbert Rd., Cleveland.

Time: Second Tuesday in October, December, February and April.

COLLEGE OF PHYSICIANS, PHILADELPHIA, SECTION ON OPHTHALMOLOGY

Chairman: Dr. Francis H. Adler, 313 S. 17th St., Philadelphia.

Clerk: Dr. W. S. Reese, 1901 Walnut St., Philadelphia.

Time: Third Thursday of every month from October to April, inclusive.

COLUMBUS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

Chairman: Dr. C. D. Postle, 240 E. State St., Columbus, Ohio.

Secretary-Treasurer: Dr. Hugh C. Thompson, 289 E. State St., Columbus, Ohio.

Place: The Neil House. Time: 6 p. m., first Monday of each month.

CORPUS CHRISTI EYE, EAR, NOSE AND THROAT SOCIETY

Chairman: Dr. F. K. Stroud, 416 Chaparral St., Corpus Christi, Texas.

Secretary: Dr. Arthur Padilla, 414 Medical Professional Bldg., Corpus Christi, Texas.

Time: Second Friday of each month from October to May.

DALLAS ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. L. A. Nelson, 4105 Live Oak St., Dallas, Texas.
 Secretary: Dr. S. F. Harrington, 921 Medical Arts Bldg., Dallas, Texas.
 Place: Dallas Athletic Club. Time: 6:30 p. m., first Tuesday of each month from October to June. The November, January and March meetings are devoted to clinical work.

DES MOINES ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. H. C. Schmitz, 604 Locust St., Des Moines, Iowa.
 Secretary-Treasurer: Dr. Byron M. Merkel, 604 Locust St., Des Moines, Iowa.
 Time: 7:45 p. m., third Monday of every month from September to May.

DETROIT OPHTHALMOLOGICAL CLUB

Chairman: Members rotate alphabetically.
 Secretary: Dr. Harvey E. Dowling, 2414 Eaton Tower, Detroit.
 Time: 6:30 p. m., first Wednesday of each month.

DETROIT OPHTHALMOLOGICAL SOCIETY

President: Dr. Parker Heath, 1553 Woodward Ave., Detroit.
 Secretary: Dr. Leland F. Carter, 1553 Woodward Ave., Detroit.
 Place: Club rooms of Wayne County Medical Society. Time: Third Thursday of each month from November to April, inclusive.

EASTERN NEW YORK EYE, EAR, NOSE AND THROAT ASSOCIATION

President: Dr. James M. Dunn, 1352 Union St., Schenectady.
 Secretary-Treasurer: Dr. Joseph L. Holohan, 330 State St., Albany.
 Time: Third Wednesday in October, November, March, April, May and June.

FORT WORTH EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. W. R. Thompson, 602 W. 10th St., Fort Worth, Texas.
 Secretary-Treasurer: Dr. A. E. Jackson, 602 W. 10th St., Fort Worth, Texas.
 Place: Medical Hall, Medical Arts Bldg. Time: 7:30 p. m., first Friday of each month except July and August.

HOUSTON ACADEMY OF MEDICINE, OPHTHALMOLOGICAL AND
 OTO-LARYNGOLOGICAL SECTION

President: Dr. Wallace W. Ralston, 1304 Walker Ave., Houston, Texas.
 Secretary: Dr. William J. Snow, 708 Medical Arts Bldg., Houston, Texas.
 Place: Medical Arts Bldg., Harris County Medical Society Rooms. Time: 8 p. m., second Thursday of each month from September to June.

INDIANAPOLIS OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President: Dr. John I. Garret, 57 Stokes Bldg., Indianapolis.
 Secretary: Dr. Kenneth L. Craft, 23 E. Ohio St., Indianapolis.
 Place: Indianapolis Athletic Club. Time: 6:30 p. m., second Thursday of each month from November to May.

KANSAS CITY SOCIETY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Homer Beal, 1103 Grand Ave., Kansas City, Mo.
 Secretary: Dr. Desmond Curran, Federal Reserve Bank Bldg., Kansas City, Mo.
 Time: Third Thursday of each month from October to June. The November, January and March meetings are devoted to clinical work.

LONG BEACH EYE, EAR, NOSE AND THROAT SOCIETY

Chairman: Dr. Harold Snow, 614 S. Pacific Ave., San Pedro, Calif.
 Secretary-Treasurer: Dr. Oliver R. Nees, 508 Times Bldg., Long Beach, Calif.
 Place: Professional Bldg. Time: Last Wednesday of each month from October to May.

LOS ANGELES SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. Harold Mulligan, 1680 N. Vine St., Los Angeles.

Secretary-Treasurer: Dr. Colby Hall, 1136 W. 6th St., Los Angeles.

Place: Los Angeles County Medical Association Bldg., 1925 Wilshire Blvd. Time: 6:00 p. m., fourth Monday of each month from September to May, inclusive.

LOUISVILLE EYE AND EAR SOCIETY

President: Dr. Joseph S. Heitger, Heyburn Bldg., Louisville, Ky.

Secretary-Treasurer: Dr. J. W. Fish, 321 W. Broadway, Louisville, Ky.

Place: Brown Hotel. Time: 6:30 p. m., second Thursday of each month from September to May, inclusive.

MEDICAL SOCIETY OF THE DISTRICT OF COLUMBIA, SECTION OF
OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman: Dr. E. J. Cummings, 1835 I St. N. W., Washington.

Secretary: Dr. P. S. Constantinople, 1835 I St. N. W., Washington.

Place: 1718 M St. N. W. Time: 8 p. m., third Friday of each month from October to April, inclusive.

MEMPHIS SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman: Each member, in alphabetical order.

Secretary: Dr. Sam H. Sanders, 1089 Madison Ave., Memphis, Tenn.

Place: Eye Clinic of Memphis Eye, Ear, Nose and Throat Hospital. Time: 8 p. m., second Tuesday of each month from September to May.

MILWAUKEE OTO-OPHTHALMIC SOCIETY

President: Dr. John B. Hitz, 411 E. Mason St., Milwaukee.

Secretary-Treasurer: Dr. Ralph T. Rank, 238 W. Wisconsin Ave., Milwaukee.

Place: University Club. Time: 6:30 p. m., second Tuesday of each month.

MONTGOMERY COUNTY MEDICAL SOCIETY

Chairman: Dr. H. V. Dutrow, 1040 Fidelity Medical Bldg., Dayton, Ohio.

Secretary-Treasurer: Dr. Maitland D. Place, 981 Reibold Bldg., Dayton, Ohio.

Place: Van Cleve Hotel. Time: 6:30 p. m., first Tuesday of each month from October to June, inclusive.

MONTREAL OPHTHALMOLOGICAL SOCIETY

President: Dr. J. Rosenbaum, 1396 Ste. Catherine St. W., Montreal, Canada.

Secretary: Dr. L. Tessier, 1230 St. Joseph Blvd. E., Montreal, Canada.

Time: Second Thursday of October, December, February and April.

NASHVILLE ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman: Dr. Andrew Hollabaugh, Doctors Bldg., Nashville, Tenn.

Secretary: Dr. Guy Maness, Medical Arts Bldg., Nashville, Tenn.

Place: St. Thomas Hospital. Time: 8 p. m., third Monday of each month from October to May.

NEW HAVEN OPHTHALMOLOGICAL SOCIETY

President: Dr. William H. Ryder, 185 Church St., New Haven, Conn.

Secretary: Dr. Frederick A. Wies, 255 Bradley St., New Haven, Conn.

NEW ORLEANS OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President: Dr. W. B. Clark, 1012 American Bank Bldg., New Orleans.

Secretary: Dr. Mercer G. Lynch, 1018 Maison Blanche Bldg., New Orleans.

Place: Louisiana State University Medical Bldg. Time: 8 p. m., second Tuesday of each month from October to May.

NEW YORK ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

Chairman: Dr. Algernon Reese, 73 E. 71st St., New York.

Secretary: Dr. Brittain Payne, 896 Madison Ave., New York.

Time: 8:30 p. m., third Monday of every month from October to May, inclusive.

NEW YORK SOCIETY FOR CLINICAL OPHTHALMOLOGY

President: Dr. James W. Smith, 1016-5th Ave., New York.

Secretary: Dr. Benjamin Esterman, 983 Park Ave., New York.

Place: Squibb Hall, 745-5th Ave. Time: 8 p. m., first Monday of each month from October to May, inclusive.

OKLAHOMA CITY ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. R. E. Leatherock, Cushing, Okla.

Secretary: Dr. Harry C. Ford, 1014 Medical Arts Bldg., Oklahoma City.

Place: University Hospital. Time: Second Tuesday of each month from September to May.

OMAHA AND COUNCIL BLUFFS OPHTHALMOLOGICAL AND
OTO-LARYNGOLOGICAL SOCIETY

President: Dr. Harold Gifford, 1620 Medical Arts Bldg., Omaha.

Secretary-Treasurer: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha.

Place: Omaha Club, 20th and Douglas Sts., Omaha. Time: 6 p. m., dinner; 7 p. m., program; third Wednesday of each month from October to May.

PASSAIC-BERGEN OPHTHALMOLOGICAL CLUB

President: Dr. L. Markowitz, 16 Church St., Paterson, N. J.

Secretary-Treasurer: Dr. A. John Reinhorn, 302 Broadway, Paterson, N. J.

Place: Paterson Eye and Ear Infirmary. Time: 9 p. m., last Friday of every month, except June, July and August.

PHILADELPHIA COUNTY MEDICAL SOCIETY, EYE SECTION

Chairman: Dr. Edmund B. Spaeth, 1930 Chestnut St., Philadelphia.

Secretary: Dr. Wilfred E. Fry, 1819 Chestnut St., Philadelphia.

Time: First Thursday of each month from October to May.

PITTSBURGH OPHTHALMOLOGICAL SOCIETY

President: Dr. J. Clyde Markel, 200-9th St., Pittsburgh.

Secretary: Dr. George H. Shuman, 351-5th Ave., Pittsburgh.

Place: Pittsburgh Academy of Medicine Bldg. Time: Fourth Monday of each month, except June, July, August and September.

READING EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. James E. Landis, 232 N. 6th St., Reading, Pa.

Secretary: Dr. Paul C. Craig, 232 N. 5th St., Reading, Pa.

Place: Wyomissing Club. Time: 6:30 p. m., third Wednesday of each month from October to July.

RICHMOND OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President: Dr. W. F. Bryce, Medical Arts Bldg., Richmond, Va.

Secretary: Dr. Richard W. Vaughan, Medical Arts Bldg., Richmond, Va.

Place: Westmoreland Club. Time: 6 p. m., second Monday of each month from October to May.

ROCHESTER EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. E. J. Avery, 11 N. Goodman St., Rochester, N. Y.

Secretary-Treasurer: Dr. Charles T. Sullivan, 277 Alexander St., Rochester, N. Y.

ST. LOUIS OPHTHALMIC SOCIETY

President: Dr. William M. James, 508 N. Grand Blvd., St. Louis.

Secretary: Dr. H. Rommel Hildreth, 823 Metropolitan Bldg., St. Louis.

Place: Oscar Johnson Institute. Time: Clinical meeting 5:30 p. m., dinner and scientific meeting 6:30 p. m., fourth Friday of each month from October to April, inclusive, except December.

SAN ANTONIO OPHTHALMOLO-OTO-LARYNGOLOGICAL SOCIETY

President: Dr. Dan Russell, 705 E. Houston St., San Antonio, Texas.
 Secretary-Treasurer: Dr. P. G. Bowen, 315 Camden St., San Antonio, Texas.
 Place: Bexar County Medical Library. Time: 8 p. m., first Tuesday of each month from October to May.

SAN FRANCISCO COUNTY MEDICAL SOCIETY, SECTION ON EYE,
EAR, NOSE AND THROAT

Chairman: Dr. Fred Boyle, 490 Post St., San Francisco.
 Secretary: Dr. Frank Hand, 450 Sutter St., San Francisco.
 Place: Society's Bldg., 2180 Washington St., San Francisco. Time: Fourth Tuesday of every month except June, July and December.

SHREVEPORT EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. David C. Swearingen, Slattery Bldg., Shreveport, La.
 Secretary-Treasurer: Dr. Kenneth Jones, Medical Arts Bldg., Shreveport, La.
 Place: Shreveport Charity Hospital. Time: 7:30 p. m., first Monday of every month except July, August and September.

SPOKANE ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Louis A. Parsell, 407 Riverside Ave., Spokane, Wash.
 Secretary: Dr. Robert L. Pohl, 407 Riverside Ave., Spokane, Wash.
 Place: Paulsen Medical and Dental Library. Time: 8 p. m., fourth Tuesday of each month except June, July and August.

SYRACUSE EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. F. R. Webster, State Tower Bldg., Syracuse, N. Y.
 Secretary-Treasurer: Dr. John R. Myers, State Tower Bldg., Syracuse, N. Y.
 Place: University Club. Time: First Tuesday of each month except June, July and August.

TOLEDO EYE, EAR, NOSE AND THROAT SOCIETY

Chairman: Dr. J. E. Minns, 316 Michigan St., Toledo, Ohio.
 Secretary: Dr. John D. Skow, 2001 Collingwood Blvd., Toledo, Ohio.
 Place: Toledo Club. Time: Each month except June, July and August.

TORONTO ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

Chairman: Dr. W. R. F. Luke, 316 Medical Arts Bldg., Toronto, Canada.
 Secretary: Dr. W. T. Gratton, 216 Medical Arts Bldg., Toronto, Canada.
 Place: Academy of Medicine, 13 Queens Park. Time: First Monday of each month, November to April.

WASHINGTON, D. C., OPHTHALMOLOGICAL SOCIETY

President: Dr. E. Leonard Goodman, 1801 I St. N. W., Washington, D. C.
 Secretary-Treasurer: Dr. Sterling Bockoven, 1752 Massachusetts Ave. N. W., Washington, D. C.
 Place: Episcopal Eye, Ear and Throat Hospital. Time: 7:30 p. m., first Monday in November, January, March and April.

WILKES-BARRE OPHTHALMOLOGICAL SOCIETY

Chairman: Each member in turn.
 Secretary: Dr. Samuel T. Buckman, 70 S. Franklin St., Wilkes-Barre, Pa.
 Place: Office of chairman. Time: Last Tuesday of each month from October to May.

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KERATOCONJUNCTIVITIS SICCA

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NEW YORK

The fact that deficient lacrimation may produce disturbances of the cornea and the conjunctiva has long been known (Wagenmann,¹ 1893). Comparatively recently (Fuchs,² 1919) it began to be suspected that the decrease in function of the lacrimal gland might be a manifestation of a systemic disturbance. In 1933 Sjögren's classic monograph^{3a} appeared, and his name is given to the syndrome of keratoconjunctivitis sicca, laryngopharyngitis sicca and enlargement of the parotid gland.

ETIOLOGY

Sometimes the cause of the diminution in lacrimal secretion is obvious. Congenital absence of the lacrimal gland has been reported by Duke-Elder⁴ and others. Lisch⁵ reported deficient lacrimation in

The loss of the original manuscript has caused some delay in the publication of this article.

From the Institute of Ophthalmology of the Presbyterian Hospital and the Department of Ophthalmology of Columbia University College of Physicians and Surgeons.

1. Wagenmann, A.: Diskussionsbemerkung, Ber. ü. d. Versamml. d. ophth. Gesellsch. **23**:172-174, 1893.

2. Fuchs, A.: Ein Fall von Fehlen der Tränen- und Mundspeichel-Sekretion, Ztschr. f. Augenh. **42**:253-256, 1919.

3. Sjögren, H.: (a) Zur Kenntnis der Keratoconjunctivitis sicca (Keratitis filiformis bei hypofunktion der Tränendrüsen), Acta ophth., 1933, supp. 2, p. 1; (b) Zur Kenntnis der Conjunctivitis sicca: II. Allgemeine Symptomatologie und Ätiologie, ibid. **13**:1-39, 1935; (c) III. Mikroskopische Veränderungen der Nasendrüsen, ibid. **13**:40-45, 1935; (d) Keratoconjunctivitis sicca—ein Teilsymptom eines grösseren Symptomenkomplexes, Ber. ü. d. Versamml. d. deutsch. ophth. Gesellsch. **51**:122-126, 1936; (e) Zur Kenntnis der Conjunctivitis sicca: IV. Mikroskopische Untersuchungen über das Initialstadium der Drüsenveränderungen, Acta ophth. **16**:70-79, 1938; (f) V. Augenveränderungen nach Extirpation der Tränendrüsen. Behandlung, ibid. **16**:80-88, 1938.

4. Duke-Elder, W. S.: Keratitis Sicca, Brit. J. Ophth. **14**:61-65 (Feb.) 1930.

5. Lisch, K.: Ueber hereditäres Vorkommen des mit Kerato-Conjunctivitis sicca verbundenen Sjögrenschen Symptomenkomplexes, Arch. f. Augenh. **110**:357-364 (March) 1937.

three generations of one family: Of 13 members examined, only 2 were free of the disease. Surgical removal of the gland has been found responsible for this condition by Wagenmann,¹ Avižonis,⁶ P. Knapp⁷ and Engelking.⁸ In a case reported by Wagenmann,¹ lacrimation ceased after a fracture of the base of the skull. Tearing has been found to have diminished after excision of the gasserian ganglion in cases reported by Engelking⁸ and Verhoeff.⁹

In most cases no such obvious cause as these has been found, and, as noted by Sjögren,³ the condition seems to be part of a general systemic disturbance. Because of the accompanying diminution in the naso-ocular reflex, catarrh of the upper respiratory tract, achylia, suppression of sweat excretion and bilaterality of the symptoms, the Dalsgaard-Nielsens¹⁰ ascribed the condition to a disturbance of the sympathetic nervous system. They expressed the opinion that the swelling of the parotid glands is the result of a secondary infection. Spector,¹¹ however, stated the belief that the sympathetic nervous system is intact. Von Grósz¹² regarded the syndrome as due to a disease of the hemopoietic system caused by avitaminosis, but this conception was refuted by Lisch.⁵ P. Knapp⁷ expressed belief that the condition is a result of acute rheumatic fever. Sjögren^{3d} pointed out that there is no evidence to support the theory of allergic-anaphylactic disturbance and stated that the condition is due to an infection carried by the blood stream. That the endocrine system may play a role in the production of the symptoms has long been suspected. In 1919 Fuchs² reported a case in which there were swelling of the parotid glands and a decrease in the flow of tears and saliva, which he considered manifestations of the menopause. Hollós (quoted by von Grósz¹²) removed the lacrimal glands from a rabbit, but keratitis did not appear until the ovaries were also removed. Krasso¹³ (quoted by von Grósz¹²) reported the onset

6. Avižonis, P.: Ueber schädliche Folgen der Tränendrüsenerntfernung, Ber. ü. d. Versamml. d. deutsch. ophth. Gesellsch. **47**:340-345, 1928.

7. Knapp, P.: Beitrag zur Frage einer schädlichen Nachwirkung der Tränendrüsensexstirpation, Klin. Monatsbl. f. Augenh. **82**:241-243 (Feb.) 1929.

8. Engelking, E.: Ueber Hornhaut- und Bindehautveränderungen infolge mangelnder Tränensekretion; Ein Beitrag zur Aetiologie der Keratitis filiformis, Klin. Monatsbl. f. Augenh. **81**:75-84 (July) 1928.

9. Verhoeff, F. H.: The Cause of Keratitis After Gasserian Ganglion Operations, Am. J. Ophth. **8**:273-275 (April) 1925.

10. Dalsgaard-Nielsen, E., and Dalsgaard-Nielsen, T.: Keratoconjunctivitis Sicca, Ugesk. f. læger **99**:219-225 (Feb. 25) 1937.

11. Spector, S. A.: Chronic Keratoconjunctivitis, Chronic Pharyngitis and Chronic Arthritis Due to Ovarian Insufficiency, Klin. med. (nos. 19-20) **9**:876-883. 1931.

12. von Grósz, S.: Aetiologie und Therapie der Keratoconjunctivitis sicca. Klin. Monatsbl. f. Augenh. **97**:472-485 (Oct.) 1936.

13. Krasso, I.: Die Behandlung der Erkrankungen des vorderen Bulbabschnittes mit Buckys Grenzstrahlen, Ztschr. f. Augenh. **71**:1-11 (April) 1930.

of keratoconjunctivitis sicca following oophorectomy. Spector¹¹ expressed the opinion that the entire picture is due to endocrine disturbance. The onset of the menopause has been considered responsible by Isakowitz¹⁴ and Hauer.¹⁵ Lisch,⁵ however, pointed out that the signs of glandular involvement may antedate the appearance of subjective ocular symptoms by several decades and that the association of the menopause with the appearance of the ophthalmic symptoms may be merely coincidental. In this connection it should be observed that several of my patients were under the age of the climacteric and that 2 of Spector's¹¹ were male. Bossalino¹⁶ stated the belief that the syndrome is due to adrenal insufficiency. In short, as Albrich¹⁷ pointed out, there is no satisfactory explanation for the condition.

Syphilis and gonorrhea were each reported only once and then in the same patient Sjögren.^{3d}

The production of keratoconjunctivitis sicca has been attributed to actual desiccation of the structures involved. Sjögren^{3a} disagreed with this theory. He expressed the opinion, based on histologic studies, that the absence of lacrimal secretion places the task of supplying moisture for the eye on the conjunctiva. This causes chronic edema, which leads progressively to hydropic degeneration and atrophy of the epithelium.

SYMPTOMS

Ocular Symptoms.—The patients complain of burning, pricking and smarting of the eyes and sometimes of diminished visual acuity. Frequently, but by no means invariably, these symptoms are accompanied by dryness. Photophobia is often present. The patients are sometimes aware of the characteristic stringy mucoid discharge and have difficulty in irrigating it away. When the mucus is adherent to the bulbar conjunctiva it stains with mild silver protein or rose bengal and can readily be seen.

Ocular Findings.—In cases of severe long-standing involvement corneal filaments are sometimes found. This occurred in only 2 of my 14 cases and in none of Spector's series of 7 cases, all of long-standing involvement. Indeed, Spector¹¹ stated the belief that the filaments previously reported were strings of mucus and pointed out, with some reason, that a dry cornea should not be expected to form vesicles.

14. Isakowitz, J.: Die endokrine Periarthritis (Umber) und Keratitis filiformis, Klin. Monatsbl. f. Augenh. **81**:85 (July) 1928.

15. Hauer, K.: Kasuistischer Beitrag zur Aetiologie der Tränendrüsenhypofunktion, Klin. Monatsbl. f. Augenh. **87**:79-81 (July) 1931.

16. Bossalino, G.: Contributo allo studio della cheratite filamentosa, Boll. d'ocul. **15**:1193-1214 (Nov.) 1936.

17. Albrich, K.: Die Keratitis filiformis und die Sekretion der Tränendrüse, Arch. f. Ophth. **121**:402-410, 1928.

In most cases the principal finding is a diffuse, irregular, superficial staining of the cornea. Often clear regions can be seen between deeply stained areas. Sensitivity is usually diminished. The eye may look dry and be flecked with meibomian secretion, but more often, as has been stressed by Sjögren^{3a} and Engelking,⁸ absence of moisture is not apparent on inspection. An almost constant finding is a thick, stringy, mucoid discharge which can be removed in the form of elastic strings. The conjunctiva may appear to be almost normal but is usually congested. A foamy secretion is often found at the canthi. The bacterial flora is generally normal.

Complications are rare. Sjögren^{3a} observed a case of pannus formation and another of perforating ulcer. In 1 of my cases a dense corneal opacity developed.

Associated Symptoms.—In the typical Sjögren syndrome the parotid glands, first one and then the other, swell gradually. The swelling is usually firm but only occasionally tender. Recessions as a rule occur in periods varying from a week to several months, but occasionally the swelling is permanent. The mouth is dry and filled with a viscid, mucoid secretion. In cases of severe involvement fissures may develop in the tongue and lips. The dryness extends to the nose, pharynx, larynx and nasal sinuses. The skin is dry, and seborrhea of the scalp is frequently observed. The patient is most uncomfortable, but the keratoconjunctivitis, which may not appear until several years after the onset of the other symptoms, seems to cause the greatest distress. One of my patients stated that her symptoms were worse during menstruation, but in Spector's¹¹ experience the reverse was true.

However, the classic picture is not always present, and, as von Grósz¹² pointed out, the ocular condition may be the only sign of a widespread systemic disturbance.

Arthritis, usually of the extremities, is frequently present. This was first described by Mulock Houwer¹⁸ but has also been reported by Sjögren^{3a} (in 17 of 22 cases), Clegg,¹⁹ Isakowitz,¹⁴ Beetham²⁰ and Wissmann.²¹ Arthritis is often absent (Medunina,²² Sjögren^{3d}) and was present in only 50 per cent of my cases.

18. Houwer, A. W. M.: Keratitis filamentosa and Chronic Arthritis, Tr. Ophth. Soc. U. Kingdom **47**:88-95, 1927.

19. Clegg, J. G., in discussion on Houwer.¹⁸

20. Beetham, W. P.: Filamentary Keratitis, Tr. Am. Ophth. Soc. **33**:413-435, 1935.

21. Wissmann, R.: Keratitis Filiformis als Teilsymptom innersekretorischer Störungen, Deutsche med. Wchnschr. **58**:1525-1527 (Sept. 23) 1932.

22. Medunina, Y. I.: Keratoconjunctivitis Due to Hypofunction of Lacrimal Glands, Vestnik oftal. **13**:655-660, 1938.

Dental caries is marked. Falling out of the teeth has been reported by Sjögren,^{3d} Deutschmann,²³ Betsch,²⁴ Wissmann²¹ and Lisch.⁵

Anemia was observed by Sjögren,^{3d} who called it simple anemia with lymphocytosis but attempted no qualitative examination. The blood picture was said by Mulock Houwer¹⁸ and von Grósz¹² to indicate the presence of pernicious anemia and by Weber and Schlüter²⁵ to be due to hypochromic anemia. The anemia was said to be gastrogenic by Wotzka (quoted by Lisch⁵).

The sedimentation rate is often increased (Sjögren,^{3d} Lisch⁵), and high values were found in some of my cases.

Sjögren^{3d} reported a case in which there were prolonged periods of a subfebrile temperature and reduced carbohydrate tolerance with normal fasting values. In a similar case Lisch⁵ observed polydipsia with no trace of disturbance in the carbohydrate metabolism.

Cyanosis of the hands and feet was reported by Weber and Schlüter.²⁵ This finding was noted in 2 of my cases.

Achylia was reported by Sjögren^{3d} and by Weber and Schlüter.²⁵ A patient of mine examined for this symptom had a positive reaction.

Achlorhydria was reported by Lisch,⁵ and "indigestion" was complained of by several of my patients. Cystitis and cholecystitis were also found in a few patients.

PATHOLOGY

The microscopic pathology has been carefully studied by Sjögren.²⁶

Conjunctiva.—There is early destruction of elastic tissue, and hydropic degeneration of the epithelium is present. Keratinization is not demonstrable. The cells are elongated. Sometimes no outlines can be observed and the epithelium has a hyaline appearance. Where this occurs goblet cells are lacking, but they are present in large numbers in the lower fornix. Scrapings may show the presence of eosinophils.

Cornea.—The epithelium is normal in some areas and thinned or absent in others. Where fibrils occur they may be formed of the external portions of the cells or of whole desquamated epithelium. Connective tissue may grow in from the limbus between the epithelium and Bowman's membrane, eventually rupturing the latter. Degenerative foci appear in the parenchyma and sometimes in the sclera.

23. Deutschmann, R.: Seltene Bindehauterkrankungen, Arch. f. Ophth. **105**: 279-285, 1921.

24. Betsch, A.: Die chronische Keratitis filiformis als Folge mangelnder Tränensekretion, Klin. Monatsbl. f. Augenh. **80**:618-623 (May) 1928.

25. Weber, F. P., and Schlüter, A.: Parotisschwellung, Xerostomie und Sjögrens Syndrom, Deutsches Arch. f. klin. Med. **180**:333-340, 1937.

26. Footnote 3 a, c, e and f.

Lacrimal Glands.—These present atrophy with connective tissue changes. In some cases the ducts show cystlike dilatation, whereas in others the parenchyma exhibits round cell infiltration with some fairly well preserved tubules. Sjögren^{3d} was unable to find giant cells in any of the cases he studied.

Parotid Glands.—When these glands were involved the primary and characteristic finding was disintegration of the glandular parenchyma. Similar changes were found in the nasal, pharyngeal and laryngeal glands. Sjögren^{3e} pointed out the similarity of this finding to those reported by Yudkin and Lambert²⁷ in the early stages of A avitaminosis.

DIFFERENTIAL DIAGNOSIS

1. *Xerophthalmia Due to A Avitaminosis.*—In most of the cases studied there was no obvious dietary insufficiency. In my most typical case biophotometry failed to reveal any lack of vitamin A.

2. *Chronic Inflammation.*—Many cases of chronic inflammation, as von Grósz¹² pointed out, are merely instances of an incomplete Sjögren syndrome. However, in most of them pathologic bacteria are found and there is no decrease in the lacrimal flow.

3. *Senile Atrophy of the Lacrimal Glands.*—This condition is likely to produce keratoconjunctivitis sicca, and as the treatment of the two diseases is the same the diagnostic point need not be stressed.

4. *Diseases Associated with Swelling of the Parotid Glands.*—When swelling of the parotid glands is present the diagnostic picture is more complicated and among the diseases to be differentiated are:

A. Mumps: According to Weber and Schlüter²⁵ this is often the first diagnosis made. The history and subsequent course make the differential diagnosis simple.

B. Calculus in Stensen's Duct: This is readily ruled out by the absence of associated symptoms and by roentgen examination.

C. Mikulicz' Disease: In the Sjögren syndrome the lacrimal glands do not swell and there is no leukemia.

D. Uveoparotid Fever: In this condition the corneal signs are absent and lacrimation is normal. Patients with Sjögren's syndrome do not have iritis.

E. Tularemia: In tularemia the systemic signs are different. The history and agglutination tests should establish the diagnosis.

F. Parinaud's Conjunctivitis: The history and the appearance are dissimilar in the two conditions, and lacrimation is normal in Parinaud's conjunctivitis.

27. Yudkin, A. M., and Lambert, R. A.: Location of the Earliest Changes in Experimental Xerophthalmia of Rats, *Proc. Soc. Exper. Biol. & Med.* **19**:375, 1922.

G. Benign Lymphoma: As Beetham²⁰ has stated, it is impossible to rule out this growth. However, most lymphomas yield to roentgen therapy, and the systemic picture is somewhat different from that encountered in the Sjögren syndrome.

H. Boeck's Sarcoid: With the exception of purpura, cutaneous lesions do not occur in Sjögren's syndrome. In all 5 of my cases in which there was enlargement of the parotid glands the reaction to the tuberculin test was negative.

MEASUREMENT OF LACRIMAL SECRETION

The lacrimal secretion is measured by a method suggested by Schirmer²⁸ in 1903. A strip of filter paper 5 mm. in width and 25 mm. in length is used. One end is placed in the lower cul-de-sac at the inner angle, covering the punctum, and the remainder is allowed to protrude between the lids. When lacrimation is normal the strip rapidly becomes moist, and the moisture is measured in millimeters from the lid margin in from one to five minutes.

This test is not particularly satisfactory. I have found that filter papers of different varieties and often different sheets of the same lot vary in absorbability when tested in my own eyes or in those of my assistants. In any event, a test with a normal eye should always be done to establish a normal measurement for each new lot of paper. It may be that the time interval of five minutes, employed by Beetham,²⁰ is too long. In my experience the normal eye will moisten the strip in from one and one-half to three minutes. When filter paper is not available the blotting paper used in the Tallqvist hemoglobin books provides a good substitute, and Spector¹¹ advocated the use of ordinary cigaret paper. Wide variations in the amount of lacrimation exist in health and in disease. Some fairly dry eyes are free from symptoms and others have been cured by being treated as dry eyes even though the blotting paper test revealed little diminution in the lacrimal secretion. It should be remembered that the blotting paper is an irritating foreign body and may excite lacrimation beyond that which is usually present.

In general, however, the filter paper test is the best test available, and it should be employed until a better one is found. In evaluating the findings experience is the best guide, and if one's own eyes are adopted as normal there will be little difficulty in detecting a diminution of the lacrimal secretion.

28. Schirmer, O.: Studien zur Physiologie und Pathologie der Tränenabsonderung und Tränenabfuhr, Arch. f. Ophth. 56:197-291, 1903.

TREATMENT

Local applications are unsatisfactory. Fibrolysin was suggested by Marchesani,²⁹ 2 per cent solution of sodium salicylate by Meisner³⁰ and egg albumin by Weve (quoted by von Grósz¹²). Von Grósz advocated the use of atropine (to increase the lysozyme concentration of tears), liquid petrolatum, physostigmine (because the symptoms resemble those of atropine poisoning) and acetylcholine. He also advised the use of artificial tears, as suggested by Gifford, and urged that acacia be added to the formula. I have used lysozyme, but without effect. Oguchi (quoted by von Grósz¹²) said that 1 per cent asparagine and 0.1 per cent benzoic acid in solution stimulated the secretion of tears. Local exposure to roentgen rays was recommended by Schall³¹ and by Krasso,¹³ but was described by von Grósz¹² and Beetham.²⁰ Löhlein³² used contact glasses.

General treatment is without effect. Liver, iron and arsenic were advised by Medunina²² and estrogens by von Grósz¹² and Spector.¹¹ Fever therapy was suggested by Flodgren (quoted by von Grósz¹²). One of Spector's patients was benefited by pancreatin.

The most satisfactory local treatment is occlusion of the puncta, as suggested by Beetham²⁰ in 1935. It should be borne in mind, however, that while closing the canaliculi is a simple matter keeping them closed is not so easy. Any procedure less complete than a thoroughgoing destruction of the canaliculi will almost certainly prove temporary in effect. Just sealing the puncta is of no value except as a temporary diagnostic occlusion. Furthermore, closure of all four canaliculi is necessary. The upper puncta are regarded as of little importance, but I have found that unless they are closed a cure will not be effected.

The canaliculus should be dilated, the diathermy or galvanocautery needle inserted as far as the entrance into the sac and the current turned on. The amount of coagulation is dependent on the current used, but experience is the best guide as to when the epithelium of the canaliculus has been destroyed. Too little exposure will be followed by recanalization of the canaliculus, whereas too active treatment will produce a somewhat disfiguring widening of the internal commissure. If properly carried out the treatment will usually result in almost instantaneous and permanent relief from ocular symptoms.

29. Marchesani, O., in discussion on Sjögren.^{3d}

30. Meisner, W.: Zur Behandlung der Keratoconjunctivitis sicca, *Ztschr. f. Augenh.* **94**:129-130 (Feb.) 1938.

31. Schall, E.: Neue Therapie der Fädchenkeratitis, *Klin. Monatsbl. f. Augenh.* **85**:406-408 (Sept.) 1930.

32. Löhlein, W., in discussion on Sjögren.^{3d}

REPORT OF CASES

CASE 1.—M. N., a Jewish housewife aged 50, was seen in the medical service of the Presbyterian Hospital on Nov. 14, 1928. She stated that her mouth had been dry for three and one-half years and that for the last two and one-half years she had had "swellings in front of her ears." These had grown, with minor recessions, for one and one-half years but in the last year had not increased in size.

The family and the personal history were irrelevant. The diet was adequate and well balanced.

Examination revealed a firm, nontender, nonfluctuating swelling of each parotid gland, the left being somewhat larger than the right and measuring 6 by 6 cm. at its most prominent area. The submaxillary glands were palpable. The lips and tongue were dry and cracked. Except to disclose paronychia on the second and fifth fingers of the left hand, physical examination gave negative results, as

TABLE 1.—*Data on Patients with the Sjögren Syndrome**

	Patients			
	M. N.	F. S.	E. T.	E. A. (Died)
Present age.....	61	40	44	34
Age at onset.....	49	38	43	30
Lacrimation.....	—	—	—	—
Dryness of mouth.....	++	+	++	+
Enlargement of parotid glands.....	+	+	+	+
Arthritis.....	+	0	0	+
Ovarian function.....	M	N	D	D
Reaction to tuberculin.....	Negative	Negative	Negative	Negative
Teeth.....	0	P	P	F
Conjunctival flora.....	N	N	N	N
Corneas.....	Fil., S.K.	S.K.	S.K.	S.K.
Visual impairment.....	+	+	++	0
Effect of ocular treatment.....	I	C	C	C

* Fil., filaments; M, menopause; D, dysmenorrhea; F, fair; S.K., superficial keratitis; N, normal; P, poor; C, cured; I, improved; —, diminished.

did neurologic consultation. Reactions to Wassermann and tuberculin tests were negative, and the blood picture showed merely a mild anemia.

After twenty-four roentgen ray treatments applied to both parotid glands, the swelling gradually disappeared, although the mouth remained dry.

In April 1929 the patient returned to report that her menses had become irregular and that at times her fingers were cold and numb. At this time the dermatologists drew attention to the dryness and scaliness of her skin. Tests for tinea produced positive reactions, and a diagnosis of trichophytosis of the fingers was made.

Roentgenograms of the skull and of the chest revealed nothing important, and the basal metabolism rate was normal. The spinal fluid was normal.

When next seen, in December 1930, the patient reported that her parotid glands had been swelling intermittently, and both glands were then enlarged. A palpable cervical gland was found under the angle of the mandible on the left side. Marked seborrhea of the scalp was also observed. The mouth was still dry, and a biopsy specimen of the gingival tissue from the lower alveolar ridge showed that the upper layer of the squamous epithelium was keratosed and the

stroma thickened. The blood vessels were dilated, and the connective tissue was edematous. There was round cell infiltration under the epithelium. About this time acute eustachian salpingitis developed, but no specific mention of dryness was made by the consultant otorhinolaryngologist. Nearly a year later, however, there developed acute pansinusitis, a peritonsillar abscess, furuncles of the auditory canal and finally acute mastoiditis on the right. At this time the otorhinolaryngologist observed that the pharynx was very dry. A simple mastoidectomy was performed. A thickened gray mucosa with a small amount of pus was found, and the patient recovered uneventfully. Purpura of the lower extremities was present, and the patient stated that the spots had appeared long before the onset of the sinusitis.

On April 29, 1931 I saw her for the first time. Examination revealed dry conjunctivas, with a stringy, mucoid discharge and a foamy secretion in the

TABLE 2.—*Values Shown by Examination of the Blood Serum of Patient M. N.*
(Case 1) Oct. 31, 1938

	Mg. per 100 Cc.	Percentage	MEq. per Liter
Carbon dioxide (content), 60.0 volumes per cent.....	25.4
Chlorides (as sodium chloride).....	610.0	...	104.3
Inorganic protein.....	3.4	...	2.0
Protein.....	...	8.9	
Albumin.....	...	2.7	7.5
Globulin.....	...	6.2	11.7
Euglobulin.....	...	2.9	150.19
Nonprotein nitrogen.....	24.0		
Sodium.....	134.4
Potassium.....	4.1
Calcium.....	8.5	...	4.3
Sugar.....	74		
Cholesterol.....	184		
Bilirubin, color +			
Phosphatase, 7.5 Bodansky units			
Acid phosphatase, 1.6 Bodansky units			

canthi. The corneas were moderately insensitive and stained throughout in a finely stippled fashion. The wearing of a patch; local applications of ethylmorphine hydrochloride, silver nitrate, Ringer's solution, cod liver oil, liquid petrolatum and lysozyme, and even removal of the epithelium proved unavailing. On May 5, 1934 typical filaments appeared for the first time on the right cornea, and later they appeared on the left.

In January 1936 the filter paper test showed almost complete absence of lacrimal secretion. The lower canaliculi were sealed, but improvement was slight. The upper canaliculi were then closed, and improvement was dramatic. The keratitis disappeared. Although reclosure had to be done on several occasions, the puncta are now permanently sealed, and the eyes, while dry, are comfortable, and the corneas do not stain.

On Nov. 3, 1938 physical examination revealed that the liver could be palpated 4 fingerbreadths below the costal margin. It was smooth. The spleen was felt 3 fingerbreadths below the costal margin. The patient reported that she had had several attacks of purpura on her lower extremities since her last examination. Studies of the serum on October 31 gave the results shown in table 2.

On June 28, 1939 the physical condition was unchanged. Laboratory reports showed that the blood contained: hemoglobin, 11 Gm. per hundred cubic centimeters; red corpuscles, 3,590,000, and white corpuscles, 4,800. The test for albumin in the urine gave a 1 plus reaction. The bromsulphalein retention was 85 per cent after five minutes and 14 per cent after half an hour. The values for the blood serum were: phosphatase, 10.5 Bodansky units; calcium, 8.8 mg. per hundred cubic centimeters; nonprotein nitrogen, 25 mg. per hundred cubic centimeters; bilirubin, a faint trace; protein, 8.3 per cent; albumin, 2 per cent; globulin, 6.3 per cent, and cholesterol, 149 mg. per hundred cubic centimeters. The venous pressure was 60 to 65 mm. Questionable ascites was noted.

Since then her status has remained approximately unchanged.

CASE 2.—F. S., a married woman aged 39, was first seen on May 7, 1937, complaining that her mouth was dry. She had always found it necessary to drink fluids with her meals, but in the last two years the dryness had become more marked. Two months before the parotid glands had become swollen, the temperature had risen to 101 F. and she had believed that she had mumps. In six weeks the swellings subsided, but two weeks before the examination the left parotid swelled again.

The family and personal history revealed nothing important. Menstruation was regular but profuse. She noticed that her mouth became much drier at the menstrual period. The diet was adequate. She stated that her teeth decayed easily and that ordinary fillings would not hold; gold inlays, however, were retained. She had had an attack of pansinusitis and threatened mastoiditis three and one-half years before and had observed that after these conditions subsided her mouth was drier.

Examination revealed that the eyes were dry. The mouth was red and dry, and a small erosion was seen in the left gingivolabial sulcus. The teeth were carious, and there were many gold fillings. Both parotid glands were enlarged and firm but not tender or fluctuating. Clear secretion was expressed by massage, and from this a culture of *Staphylococcus aureus haemolyticus* was obtained. The submaxillary nodes were palpable but not tender. Otherwise physical examination gave negative results.

Roentgenograms of the sinuses, lungs and parotid regions showed all these to be normal. Basal metabolism, Wassermann and tuberculin tests gave negative results.

The blood picture was as follows: hemoglobin, 90 per cent; red corpuscles, 4,500,000; white corpuscles, 6,500; polymorphonuclear leukocytes, 57 per cent; lymphocytes, 27 per cent; mononuclear leukocytes, 2 per cent; eosinophils, 4 per cent; sedimentation rate, 56 mm. in an hour; slight anisocytosis and polychromasia.

The dark adaptation was tested by Dr. Selig Hecht, who reported that the vitamin A content and utilization were apparently normal.

On December 7 there was renewed swelling of both parotid glands, which subsided after four treatments with diathermy. The physical condition was otherwise unchanged.

The patient's eyes were first examined on March 17, 1939. She was then 40 years old. She stated that her eyes had been red and sore for about two years, but she did not complain of dryness until specifically questioned, when she admitted that her tears were scanty. Vision was 20/15— in each eye with her mixed astigmatic correction. On inspection the conjunctivas did not appear particularly dry, but by the Schirmer test little lacrimation was found. Stringy mucus was

seen in the lower retrotarsal folds, and white foamy secretion was present at all the canthi. The corneas stained irregularly and superficially with fluorescein. No filaments were seen. The conjunctival flora was normal. The puncta were temporarily occluded, and three days later the patient returned to report what she called an "amazing" recovery. In a few days the puncta became patent again, and all were then sealed permanently. When she was last seen, on Jan. 12, 1940, she was free of ocular symptoms.

CASE 3.—E. T., a single woman aged 44, was seen first on Jan. 4, 1940. She complained that two years before her parotid glands had swollen simultaneously without apparent cause and that her mouth had become dry. One year before the eyes had become red, sore and dry, and lately the vision was becoming blurred. Local treatment had proved unavailing.

Recently she had noticed indefinite pain in the joints of her extremities. The menstrual flow, previously normal, had been scanty for the last month or so, and

TABLE 3.—*The Blood Picture of 4 Patients with the Sjögren Syndrome*

Patient	Hemo- globin, Per- cent- age	Red Blood Cells	White Blood Cells	Poly- mor- phonu- clear Leuko- cytes, Per- cent- age	Lym- pho- cytes, Per- cent- age	Mono- nu- clear Leuko- cytes, Per- cent- age	Eosin- ophils, Per- cent- age	Erythro- cyte Sedi- menta- tion Rate	Platelets	Morphologic Aspect
M. N.	76	3,590,000	4,800	78	15	5	0	121	89,000	Polychromasia; anisocytosis
F. S.	90	4,500,000	6,500	57	27	2	4	56	Polychromasia; anisocytosis
E. T.	98	4,470,000	7,550	75	20	3	2	24	290,000	
E. A.	79	3,800,000	3,000	42	47	6	1	75	199,000	Achromia; anisocytosis
7/8/37										

she had uterine pain between periods. The teeth had lately become "soft" and retained fillings poorly.

Examination revealed that she had a firm, not particularly tender, bilateral and equal swelling of the two parotid glands. The tongue and the pharynx were red and dry. Otherwise investigation gave negative results, and the patient stated that a complete examination in a diagnostic clinic and at Mount Sinai Hospital had also proved fruitless.

The blood picture was as follows: hemoglobin, 98 per cent; red corpuscles, 4,470,000; white corpuscles, 7,550; polymorphonuclear leukocytes, 75 per cent; lymphocytes, 20 per cent; mononuclear leukocytes, 3 per cent; eosinophils, 2 per cent; sedimentation rate, 24 mm. in an hour; platelets, 290,000.

Examination of the eyes showed that the vision without correction was 20/100 in the right eye and 20/100 in the left and that the conjunctivas were dry and congested. Sticky, elastic mucoid strings were present in the lower retrotarsal folds. The corneas stained irregularly and superficially over their entire surfaces, but no filaments were seen. The lacrimal secretion was markedly diminished. Bacteriologic examination revealed the presence of normal flora.

On January 9 all canaliculi were sealed throughout their length by the actual cautery. The next day the eyes were moist, and two days later the vision in each eye was 20/20. There has been no recurrence of the ocular symptoms.

CASE 4.—E. A., a woman aged 32, was first seen on Dec. 5, 1936. For the last two years there had been recurrent purple blotches on the feet and ankles. These appeared suddenly, reached a maximum in twelve hours and passed away in seventy-two hours without leaving any trace. The onset was marked by burning but not by itching. For seven years she had experienced recurrent swelling of the parotid glands, first on one side and shortly after on the other. Sometimes during these attacks she would have a low grade fever. Since the first attack the mouth had been dry, but during the attacks it was much drier. Each attack lasted only a few days. The nose, throat and skin were so dry that she had to apply oil to them in order to be comfortable. The eyes had been red and sore for several years. She was unaware that they were dry until recently, when, after the death of her dog, she cried hard but no tears appeared.

The family history was irrelevant. The personal history revealed what she called "poor digestion" but otherwise nothing important. Except for mild discomfort between periods—*Mittelschmerz*—menstruation was normal.

TABLE 4.—Values Shown by Examination of the Blood Serum of Patient E. A. (Case 4)

	Mg. per 100 Cc.	Percentage	MEq. per Liter
Carbon dioxide (content), 57.8 volumes per cent.....	24.3
Chlorides (as sodium chloride).....	632.0	...	108.0
Inorganic protein.....	2.8	...	1.6
Protein.....	8.0	
Albumin.....	3.9	10.7
Globulin.....	4.1	
Euglobulin.....	1.5	
Nonprotein nitrogen.....	33.0		
Sodium.....	139.1
Potassium.....	4.3
Calcium.....	9.4	...	4.7
Cholesterol.....	200		
Phosphatase, 2.8 Bodansky units			

Examination disclosed an irregular violaceous macular rash extending from the hip to the foot on both legs. Most of the maculas were 2 by 4 mm. in size, but many were confluent, the largest being 8 by 10 cm. The anterior patellar regions and the lateral knee regions were tender to pressure. The throat was dry and congested; the tonsils were cryptic and adherent. The sense of smell was defective, and there was some postnasal dripping. The teeth showed numerous fillings but were in good condition. The physical examination otherwise gave negative results.

Examination of the blood showed: hemoglobin, 61 per cent; red corpuscles, 3,700,000; white corpuscles, 4,500; polymorphonuclear leukocytes, 42 per cent; lymphocytes, 52 per cent; sedimentation rate, 76 mm. in an hour; platelets, 143,000; slight achromia and anisocytosis.

Examination of the blood serum gave the results shown in table 4.

The Wassermann reaction was negative with both antigens; the electrocardiogram was normal. A culture of material from the throat contained staphylococci (*Staph. aureus*) and pneumococci of type 21 equally distributed. The agglutination test for streptococci gave a positive reaction with a dilution of 1:160.

On December 5 the eyes were examined. The vision was 20/20 in the right eye and 20/40 in the left, corrected 20/20 in each eye with glasses. The

parotid glands were full but not definitely swollen and not tender. The mouth was slightly dry. The Schirmer test showed marked diminution of the lacrimal secretion. The conjunctivas were congested. Much sticky, stringy mucus was found in each retrotarsal fold below. The lid margins were reddened, but there was no desquamation. The corneas were somewhat insensitive and stained widely in an irregular fashion over their entire surfaces. No vesicles or filaments were seen. The interiors were normal. Conjunctival smears were essentially negative.

The puncta were occluded temporarily, and when the patient reported improvement they were closed permanently. Later she returned to report that she was free of ocular symptoms for the first time in years. When she was last seen in the ophthalmic department, on July 8, 1937, her symptoms had disappeared entirely.

On May 23, 1938 she returned to her physician complaining of pain in her knees and wrists. The blood picture at this time was hemoglobin, 84 per cent; red corpuscles, 4,120,000; white corpuscles, 5,180; polymorphonuclear leukocytes, 27 per cent; lymphocytes, 66 per cent; mononuclear leukocytes, 7 per cent; sedimentation rate, 80 mm. in an hour. Physical examination gave negative results.

On June 26 she entered the hospital with an acute ileus, and she died three days later with septicemia due to colon bacilli.

Autopsy unfortunately did not include examination of lacrimal or parotid glands. The picture was clouded because of the septicemia, but, since this is the first autopsy recorded in a case of the Sjögren syndrome, the observations are abstracted here.

Macroscopic Examination.—Peritoneal Cavity: About 1,000 cc. of blood-tinged fluid was removed. The liver was at the level of the xiphoid process, and the spleen was above the costal margin. The intestine was markedly dilated, covered with yellowish exudate in the suprapubic region and adherent to the anterior abdominal wall. The mesenteric glands were not enlarged.

Thoracic Cavity: There was 250 to 300 cc. of clear brown fluid in each hemithorax. No pulmonary embolus was found.

Heart: A few milk plaques on the anterior surface of the right ventricle constituted the only unusual observation.

Lungs: The inferior lobes were compressed, firm and red.

Spleen: The weight was 80 Gm. and the measurements 10.5 by 7 by 3.5 cm. The capsule was violaceous and wrinkled and in consistency soft and boggy. The trabeculae and the malpighian follicles were prominent. The cut surface was brick red.

Liver: The weight was 1,450 Gm. and the measurements 26 by 22 by 7 cm. There were light yellow areas scattered through the tissue beneath the capsule.

Gallbladder and Pancreas: These were normal.

Adrenals: These glands were normal in size, shape and position. The cut surface showed a decrease in the cortical lipid.

Kidneys: The right kidney weighed 140 Gm. and measured 11.5 by 6.5 by 3.5 cm.; the left weighed 160 Gm. and measured 12.5 by 7.5 by 4.5. They were pale and turgid, with dilated venules on the surface. The vascular markings of the cortex were increased, and there were occasional tiny hemorrhagic areas at the junction of the cortex and the medulla.

Pelvic Organs: These were normal.

Alimentary Tract: The tract was normal to a point 16 cm. proximal to the ileocecal valve. Here there was partial necrosis of the bowel, with the serosal

surface covered by thick yellowish exudate. The process extended to the ileocecal valve.

Neck Organs: These organs were normal.

Bone Marrow: The bone marrow was normal.

Brain: There was moderate congestion of the small leptomeningeal vessels over the convexity bilaterally. Otherwise the brain was normal.

Bacteriologic Report.—The heart's blood contained colon bacilli.

Microscopic Examination.—Heart: There was an increased deposition of collagen about the muscle bundles. In one, capillary necrosis of the wall, fibrin production and mononuclear wandering cells were seen.

Lung: In the interstitial tissues, chiefly about the bronchioles and larger vessels, there were noted engorgement of the vessels and infiltration with round cells and some polymorphonuclear cells. There were areas of patchy pneumonia, characterized by collections of fibrin and red cells in the alveoli. Both gram-negative and gram-positive bacilli were observed, the former large and single and the latter smaller and in pairs. A few gram-positive cocci were also seen.

Spleen: The pulp was engorged with red cells, which chiefly were confined to the sinuses but occasionally infiltrated the surrounding tissues. The malpighian bodies were diffuse and invaded by collagen fibers and contained a few lymphocytes and an occasional polymorphonuclear cell.

Liver: Except for diffuse vacuolization in the areas near the portal radicles, the liver was essentially normal.

Pancreas: The pancreas was normal.

Adrenals: There was a marked decrease in the cortical lipid material.

Kidneys: Many of the glomerular tufts showed slight thickening of the basement membrane, and between them and the capsule there was protein precipitate. There was cloudy swelling, but there were no casts.

Ovaries, Uterus, Thyroid: These were normal.

Ileum: The essential lesion was a necrotizing ileitis affecting the lower 2 or 3 feet (60 or 90 cm.) of ileum.

Vertebrae, Sternum: Nothing abnormal was seen.

Brain: Except for congestion of the parenchyma of the frontal lobe, the corpus striatum, the leptomeninges and the vessels on the floor of the fourth ventricle, the brain was essentially normal.

CASE 5.—M. C., an Italian housewife aged 30, was seen first on March 10, 1939. She complained that eighteen months before she had begun to have generalized headaches and noticed that her fingers became numb and pale when exposed to cold. She had also experienced mild migratory joint pains, particularly in the wrists and knees.

The family and personal history revealed nothing important.

Physical examination gave practically negative results. The spleen was barely palpable. The fingers became blanched and painful when placed in cold water and dusky and painful when placed in warm water.

The laboratory reports showed: urine, normal; Kline reaction, negative; basal metabolic rate, —5; antistreptolysin titer, 250; reaction to the agglutination test for streptococci, negative; Mantoux reaction, slightly positive; reaction to the intracutaneous test with Brucella vaccine and to the Frei test, negative. The blood picture was: hemoglobin, 12 per cent; red corpuscles, 4,700,000; white corpuscles, 8,850; polymorphonuclear leukocytes, 79 per cent; lymphocytes, 17 per cent; mononuclear leukocytes, 4 per cent; sedimentation rate, 74 mm. in an hour.

The electrocardiogram showed nothing significant. The values for the blood serum were: protein, 8 per cent; albumin, 4.3 per cent; globulin, 3.7 per cent; euglobin, 7 per cent; nonprotein nitrogen, 26 mg. per hundred cubic centimeters. Agglutination tests for *Brucella abortus* and *Brucella melitensis* produced negative reactions. A culture of material from the throat was negative. Skeletal roentgenograms revealed nothing abnormal.

The eyes had been examined first on Oct. 17, 1938. The patient complained that for about a year the eyes had smarted and burned and that she did not see so well as formerly. The vision was 20/100 in the right eye and 5/200 in the left, improved to 20/50 in the right eye and to 20/100 in the left. She said that the left eye had never been so good as the right.

The conjunctiva was congested, and stringy mucus was found in the lower cul-de-sac. With fluorescein the corneas stained widely and irregularly over their entire surfaces. No filaments were seen. By the Schermer test lacrimation was found to be greatly lessened. Sensitivity was diminished. The interiors

TABLE 5.—Data on Ten Patients with Keratoconjunctivitis Sicca *

	M. C.	S. C.	C. F.	S. K.	L. G.	P. K.	M. R.	W. D.	G. M.	B. E.
Present age.....	31	71	62	56	38	52	68	68	20	61
Age at onset.....	30	68	55	53	35	48	65	65	17	60
Lacrimation.....	—	—	—	—	—	—	—	—	—	—
Dryness of mouth.....	+	0	+	+	0	+	+	0	0	0
Enlargement of parotid glands.....	+	0	0	0	0	0	+	0	0	0
Arthritis.....	+	0	0	+	0	+	+	—	0	0
Ovarian function.....	D	P.M.	P.M.	P.M.	N	M	P.M.	P.M.		
Conjunctival flora.....	N	N	N	N	N	N	N	N	N	N
Corneas.....	S.K.	S.K.	S.K.	S.K.	S.K.	S.K.	S.K.	S.K.	Op. S.K.	S.K.
Visual impairment.....	+	+ F.	Sl.	Sl.	0	Sl.	Sl.	0	++	0
Effect of treatment....	C	C	C	C	C	C	C	C	0	I

* N, normal; D, dysmenorrhea; —, diminished; C, cured; M, menopause; S.K., superficial keratitis; Op., corneal opacity; I, improved; P.M., postmenopause; F, filaments; —, no record made; Sl., slight; F, fundus lesion cause of visual impairment.

were normal. The conjunctival flora was normal. On Oct. 30, 1939 the puncta were closed temporarily, and the next day no corneal staining was observed. The patient manifested no symptoms. On November 14 the canaliculi were closed permanently, and on December 5 the vision was 20/40 in the right eye and 20/70 in the left with correction. On December 18, when last seen, she reported that her eyes were entirely comfortable.

CASE 6.—S. K., a housewife aged 53, was first seen on Feb. 12, 1940, complaining that for the last two years her eyes had burned and that she had had a feeling of sand in both eyes. For several years her nose and throat had been dry, and she had also had some pain in her joints.

With the exception of occasional "gallbladder attacks" which had necessitated drainage, the history revealed nothing important, and the general physical examination gave negative results.

The vision with correlation was 20/15 in the right eye and 20/30 + in the left. The eyes did not appear particularly dry, but by the Schirmer test the secretion was found to be diminished. The cornea stained in a fine punctate fashion over

its entire area. Otherwise the eyes were normal. The conjunctival flora was normal.

On February 16 the canaliculi were permanently occluded. Three days later the patient was free of symptoms, and the relief has persisted to the time of writing.

CASE 7.—S. C., a widow aged 71, was seen first on Nov. 20, 1939. She complained that for two and one-half years her eyes had felt as though there were sand in them. Recently her symptoms had grown much worse.

The family history was irrelevant. The personal history revealed that she had had a low grade cystitis for three years and that the appetite had been poor for years. The appendix had been removed in 1921.

The physical condition, except for coldness of the extremities, was essentially normal. The blood pressure was 180 systolic and 30 diastolic.

Neurologic examination gave negative results. Roentgenograms revealed periodontoclasia and also a small osteoma of the hard palate.

The blood picture was: hemoglobin, 84 per cent; red corpuscles, 4,090,000; white corpuscles, 7,000; small lymphocytes, 22 per cent; large lymphocytes, 1 per cent; mononuclear leukocytes, 6 per cent; polymorphonuclear neutrophils, 68 per cent; basophils, 1 per cent; band forms, 2 per cent.

A test of the urine for dextrose gave a 1 plus reaction. The conjunctival flora was normal.

Examination of the eyes showed the vision to be 20/30 in the right eye, improved to 20/25, and 20/50 in the left eye, unimproved. Foamy secretion was observed at the canthi, and frequent blinking was noted. The conjunctivas were congested, and the corneas showed many superficial staining areas. No filaments were seen. There was nuclear sclerosis of each lens, and stringy vitreous opacities, colloid degeneration around each macula and moderate retinal arteriosclerosis were present. The Schirmer test revealed almost no wetting of the paper.

On November 27 the canaliculi were occluded by electrocoagulation, and when last seen the patient was free of irritative symptoms.

CASE 8.—C. F., a widow of 58, was first seen on June 23, 1936. She complained that for about three years her eyes had burned and felt tired. The sensation was present constantly but was rendered worse by reading. About the time that the eyes became troublesome, the mouth became dry.

The family history was irrelevant. The personal history showed that the menses had ceased after hysterectomy for a fibroid growth seven years before. Twenty-five years before she had had acute articular rheumatism for three months, and several attacks of auricular fibrillation had occurred in the last four years.

Physical examination revealed the presence of auricular fibrillation and arteriosclerotic heart disease. This was confirmed by the electrocardiogram. Laboratory reports showed: albumin in the urine, 1 plus; Wassermann reaction, negative; basal metabolic rate, normal. The report on the blood showed: hemoglobin, 90 per cent; red corpuscles, 4,530,000; white corpuscles, 7,500; polymorphonuclear leukocytes, 68 per cent; lymphocytes, 21 per cent; mononuclear leukocytes, 9 per cent; eosinophils, 2 per cent; sedimentation rate, 50 to 86 mm. in an hour; smears, normal.

The serum contained: total protein, 6.9 per cent; albumin, 3.9 per cent; globulin, 3 per cent.

Roentgen examination showed the gallbladder region to be normal.

Examination of the eyes showed that the vision with correction was 20/30 in the right eye and 20/20— in the left. The conjunctivas were congested. Foamy secretion was present in the canthi, and strings of sticky mucus were found in the lower retrotarsal folds. The corneas stained in a punctate fashion, chiefly over the centers, and sensitivity was reduced. By the Schirmer test the lacrimal secretion was found to be scanty. The interiors were normal.

On July 28 the puncta were all closed temporarily. On August 7 there was no corneal staining, the eyes were comfortably moist and the vision in each eye was 20/20+. Closure of the puncta was then made permanent, and when last seen, on July 3, 1937, the patient had no ocular symptoms.

CASE 9.—G. M., a schoolboy aged 17, was first seen on June 21, 1937. He stated that since a severe attack of scarlet fever the previous fall his eyes had been sore and he had suffered greatly on exposure to light. His general health was excellent, and a recent physical examination was said to have given negative results. The Wassermann reaction was negative. The diet was adequate.

Examination revealed the presence of much photophobia, with the vision 20/100+ in each eye. Refraction was not done. The conjunctivas were congested, and the filter paper was not moistened at all after several minutes in the lower culs-de-sac. The corneas stained irregularly and superficially, and sensitivity was decreased. The conjunctival flora was not investigated, as repeated bacteriologic examinations elsewhere were said to have given negative results.

The puncta were occluded, and the patient was returned to his physician in the West with the suggestion that the ducts be closed permanently. He was comfortable for a while, but later his symptoms were said to have recurred. I did not see him again until three years later. The canaliculi were then apparently closed, but the eyes were still somewhat dry and the vision had been seriously reduced by interstitial vascularization and superficial central corneal opacity.

CASE 10.—L. G., a housewife aged 35, was seen on Sept. 25, 1937. She complained that for the last three years her eyes, particularly the left one, had been painful and red. Her general health was good, and physical examination was said to have given negative results.

Examination of the eyes revealed that the vision with correction was 20/20 in the right eye and 20/20— in the left. The conjunctivas were congested, but the flora was normal. The left cornea showed superficial areas of staining over the entire surface. The right cornea was normal. Lacrimation in the left eye was markedly diminished. On April 2, 1938, local treatment having proved futile, the canaliculi of the left eye were occluded. It was necessary to repeat the closure on two subsequent occasions, but when the patient was last seen, on July 22, 1939, she was comfortable.

CASE 11.—P. K., a housewife aged 52, was first seen on Jan. 8, 1940 complaining that for the last four years she had had the sensation as of a foreign body in each eye. She had consulted many oculists, but without obtaining relief.

The personal history disclosed that she had had multiple arthritis and some cholecystitis. The mouth was dry. The results of general physical examination were said to have been negative.

Examination of the eyes showed dried secretion in the inner canthi. The palpebral conjunctivas were injected, and there was mucus in the lower culs-de-sac.

Innumerable areas of superficial staining were seen over both corneal surfaces. Otherwise the eyes, including the flora, were normal.

On March 18 the canaliculi were occluded. Improvement was immediate, and when last seen the patient was entirely comfortable.

CASE 12.—M. R., a housewife aged 65, was first seen on Feb. 9, 1937 complaining that her eyes had been dry and "sticky" for about a year. Two years before, after an intestinal upset, her mouth had become dry, and simultaneously her parotid glands had swelled. The latter had been treated by three exposures to roentgen rays, but these had caused the swellings to increase.

The patient had been suffering from cholecystitis and multiple arthritis for twenty-five years. The blood sugar content, the blood urea content and the urine were normal. The Wassermann reaction was negative and the basal metabolic rate —12. The mouth was dry and the tongue fissured.

Examination of the eyes revealed the vision to be 20/20— in each eye with correction. The conjunctivas were congested, and elastic strings of mucus were found in the lower cul-de-sacs. The corneas stained superficially over their entire surfaces.

On February 12 the puncta were closed temporarily. The patient was comfortable for three weeks, after which her symptoms recurred. The canaliculi were

TABLE 6.—*Result of Treatment (All Cases)*

Patient cured.....	79 per cent
Patient improved.....	14 per cent
Patient unimproved.....	7 per cent

then occluded permanently, and when last seen, on March 24, 1937, she was entirely comfortable.

CASE 13.—W. D., a widow aged 66, was first seen on Sept. 27, 1937 complaining that for the last year her eyes had felt irritated. Her mouth, throat and nose had been dry for an undetermined period. Except for an indefinite history of anemia of unstated type and of cystitis the general history revealed nothing important.

Ocular examination revealed subacute conjunctivitis in both eyes, with superficial staining of the right cornea. The left cornea did not stain. Cultures of specimens from the conjunctiva revealed many rodlike forms resembling the Morax-Axenfeld bacillus. Lacrimation in both eyes was diminished. On November 23 the left canaliculi were occluded. Ten days later the patient reported that she felt much better, and when she was last seen, on Oct. 6, 1939, her eyes were comfortable but she stated that multiple arthritis had developed.

CASE 14.—B. E., a gardener aged 61, complained that for about a year his eyes had felt irritated and that light annoyed him excessively. His personal history was irrelevant, and a complete physical examination was said to have given negative results.

The vision with correction was 20/15 in the right eye and 20/30 + in the left. The conjunctivas were congested, and mucus was present in the lower cul-de-sacs. The corneas stained superficially over the entire surfaces, and an occasional

short filament was seen. Lacrimation was markedly diminished. The conjunctival flora was normal. The results of ocular examination were otherwise negative.

The canaliculi were closed with the actual cautery, and since then the patient has been relatively free of irritative symptoms.

SUMMARY

Deficient lacrimation may produce a troublesome keratoconjunctivitis. When this is associated with pharyngitis sicca, xerostomia and swelling of the parotid glands (the Sjögren syndrome), the condition is easily diagnosed. When, however, obvious systemic disorders are absent, there may be failure to recognize the true nature of the disease.

Four cases of the Sjögren syndrome and 10 cases of keratoconjunctivitis sicca without marked systemic derangement are reported. The diagnosis and an effective method of treatment are discussed.

SOCKET RECONSTRUCTION

A NEW FORM AND METHOD OF HANDLING THE SKIN GRAFT

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HEMPSTEAD, N. Y.

Some of the most distressing cases cosmetically are those in which a socket is so deformed that an artificial eye cannot be worn (fig. 1). Little of importance has been added to the technic of socket reconstruction since the publication of papers by J. F. S. Esser¹ and John M. Wheeler.² The purpose of this paper is to present some newer points in the technic which have proved satisfactory. For a discussion of the general technic of preparation of the socket the reader is referred to the

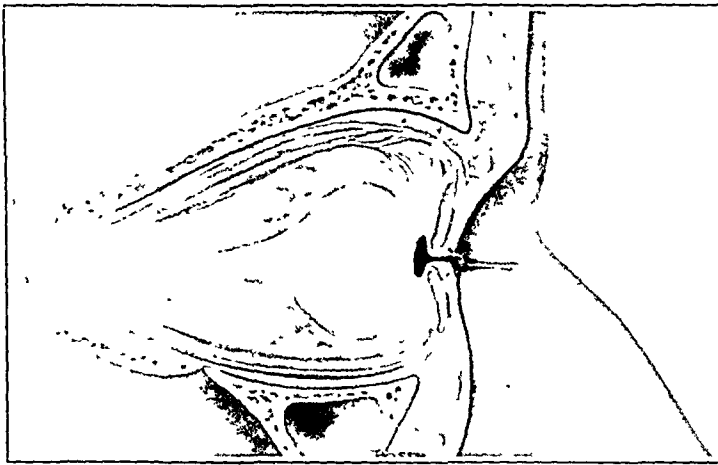


Fig. 1.—Cross section of the contracted socket.

article by John M. Wheeler published in 1921.^{2b} The preparation of the bed and the taking of the graft are fully described.

The new developments are (1) the form around which the Thiersch graft is wrapped and (2) the method of handling the graft.

The new form is concavoconvex (fig. 2) instead of biconvex, like that described by the two authors mentioned. The purpose of the new shape is self evident, viz. to provide a form that will more nearly conform to the shape of the socket it is desired to create. The biconvex form formerly used tends to depress the central portion of the posterior wall

1. Esser, J. F. S.: Epithelienlage als konjunktivaler Ersatz, *Klin. Monatsbl. f. Augenh.* **63**:374 (Sept.) 1919.

2. Wheeler, J. M.: (a) *Ohio State M. J.* **15**:455-600 (July) 1928; (b) *Am. J. Ophth.* **4**:481-488 (July) 1921.

of the socket more than the periphery, while this wall should ideally be convex forward to conform to the shape of the artificial eye to be worn. The lateral and the medial canthus can be constructed to better advantage, since the form dips backward to increase the room pro-

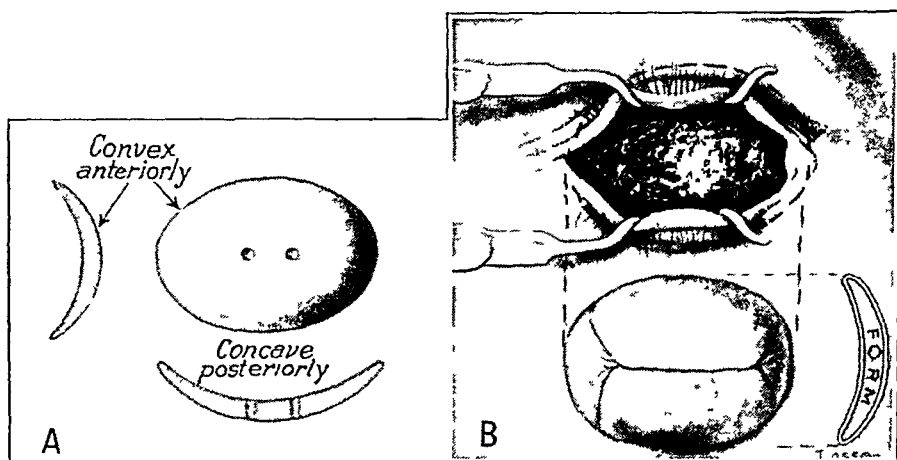


Fig. 2—*A*, the concavoconvex form, full and sectional views. *B*, the socket dissected and the form wrapped and ready to be inserted.

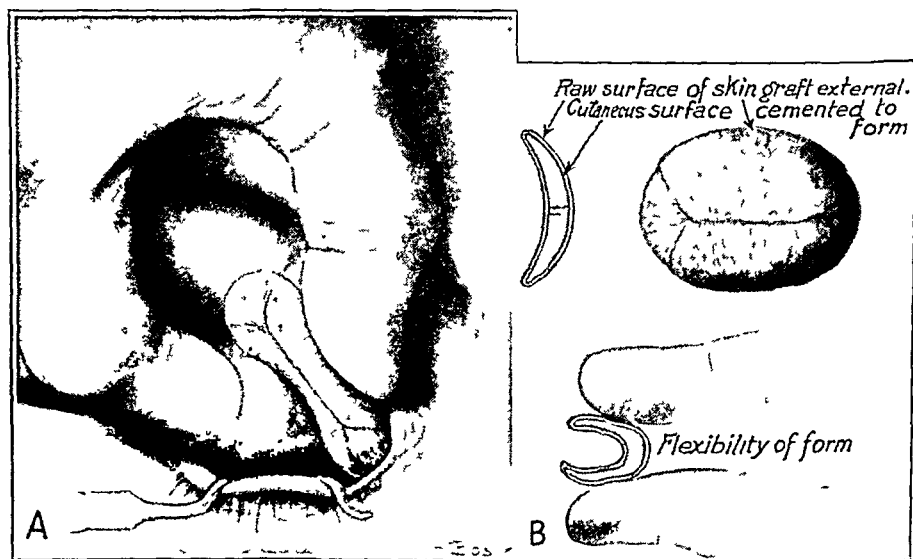


Fig. 3.—*A*, the wrapped form folded for the purpose of insertion. *B*, the form with the cutaneous surface of the graft cemented to it, showing its flexibility.

vided in the new socket for the ultimate reception of the prosthesis and for its rotation.

The form is flexible to enable its insertion to be made without undue enlargement of the interpalpebral fissure by a large canthotomy, such as

is necessary for the insertion of any rigid form of similar dimensions (fig. 3). There are two holes in the graft to facilitate handling it (figs. 2 A and 5), especially in removing it at the end of twelve to fifteen days. The form is of sufficient thickness to regain and retain its shape after insertion.

The thin dermoepidermic graft removed from the leg is held in place on the form by means of rubber cement. A layer of rubber cement is

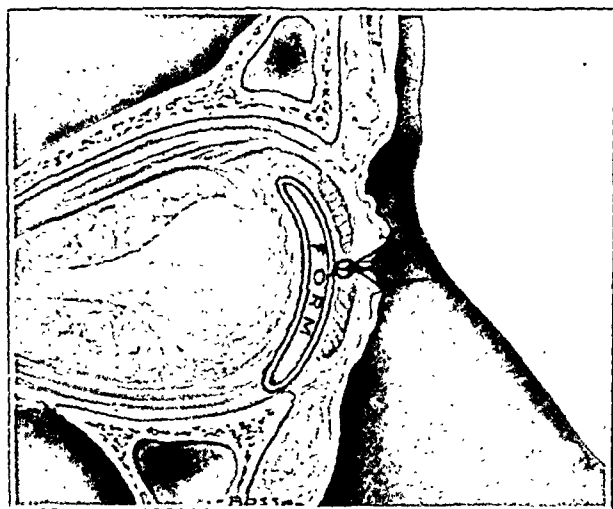


Fig. 4.—Cross section of the wrapped form inserted into the prepared socket.

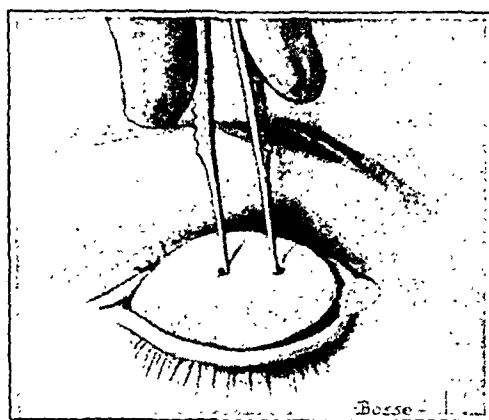


Fig. 5.—Method of removal of the form.

applied to the form, and it is set aside for five to ten minutes to dry. The form is placed on the skin, which is spread out evenly on a piece of gauze or a towel stretched over a flat surface. The under surface is firmly pressed down against it. More cement is then applied to the skin surrounding the form and allowed to dry. The skin is folded around the margins and over the anterior convex surface of the form, to which

it adheres (figs. 2 *B* and 3). The excess skin is trimmed off, and the form is inserted into the prepared socket (fig. 4).

A mattress suture is applied to the under surface of the lids near their margins to draw them together over the wrapped form.

A pressure dressing is applied and left in place for five days to a week. The dressing is changed every four or five days for three weeks. The form is not removed for two weeks. It is lifted out readily by means of a Lester forceps passed into the holes to elevate the lower margin (fig. 5). The socket is ready for a prosthesis at the end of three or four weeks.

The skin cannot permanently adhere to the form, since the superficial layers desquamate and become necrotic, thus releasing the form.

The forms can be made any desired shape and further trimmed with scissors in special cases. If one is handy with heavy scissors several forms can be made from a hollow rubber ball about the size of a tennis ball. The edges are smoothed and thinned down on an emery wheel.

OCULAR MANIFESTATIONS IN MYASTHENIA GRAVIS

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Myasthenia gravis, so named by Jolly¹ in 1895, is clinically characterized by a syndrome which includes weakness, fatigue and in some cases actual wasting away of muscles without any pathologic changes microscopically demonstrable as specific to the disease.

There seems to be a predisposition for involvement of groups of muscles innervated by cranial nerves.

The causation is unknown, but it is believed that there is such an insufficiency of acetylcholine or some like substance at the myoneural junction that the neuromotor impulse is not transmitted across the junction. It has been postulated that this fault is caused either by underproduction of the choline-like substance at the motor end plates or by an accelerated disposal of it by an overabundance of acetylcholine esterase, a substance whose normal function is to destroy acetylcholine.²

This disease is no regard of sex, approximately equal numbers of males and of females being affected.

There are no age limits, but most patients are in the second to the fifth decades inclusive.

No predisposing factors are known, but pregnancy has been observed to alter the course of the disease. In the Massachusetts General Hospital series, 3 of 4 patients improved during gestation. Wilson,³ referring to his own patient and to the patients of Goldflam and Laurent, noted improvement in the myasthenic course in 2 patients who became pregnant, but Tilney, Cohen and others noted the opposite effect.

Possibly the disturbed creatine-creatinine balance, with creatinuria, described by Boothby⁴ is a reflection of abnormal muscle physiology rather than a factor in the cause of myasthenia gravis.

Read before the New England Ophthalmological Society, Dec. 17, 1940.

From the Department of Ophthalmology, Massachusetts Eye and Ear Infirmary; as paper number 14, from the Myasthenia Gravis Clinic of the Department of Neurology, Massachusetts General Hospital. and from Harvard Medical School.

1. Jolly, F.: *Berl. klin. Wchnschr.* **32**:33 and 248, 1895; cited by Wilson.³

2. Monrad-Krohn, G. H.: *The Clinical Examination of the Nervous System*, ed. 7, New York, Paul B. Hoeber, Inc., 1937, pp. 185-186.

3. Wilson, S. A. K.: *Neurology*, Baltimore, William Wood & Company, 1940, vol. 2, pp. 1595-1607.

4. Boothby, W. M.: *Myasthenia Gravis*, *Proc. Staff Meet., Mayo Clin.* **7**:557-562 (Sept. 28) 1932.

A review of the more recent ophthalmic literature revealed a paucity of information pertaining to this subject, and it was felt that a report such as this might be useful. Painstaking reviews of the older general literature on myasthenia gravis have been made by several of the authors referred to.

Through the cooperation of Dr. Henry R. Viets and Dr. Robert S. Schwab, 26 cases chosen at random from the Myasthenia Gravis Clinic of the Massachusetts General Hospital were made available for this study.

SYMPTOMATOLOGY

Muscular fatigue is a frequent early symptom, but ordinarily the patient first complains to the physician of muscular weakness, whether

Statistics on External Ocular Signs and Symptoms

Signs and Symptoms	Number of Patients	Percentage
Number of patients in series.....	26	
Ocular symptoms at some time during the course of the disease....	25	96+
Diplopia on one or more occasions.....	23*	90—
Ptosis on one or more occasions.....	22†	85+
Diplopia and ptosis simultaneously on some occasions.....	20	77—
Some ocular symptom as the first subjective indication of the disease	17	65+
Ptosis as the first subjective indication.....	12	46+
Diplopia as the first subjective indication.....	9	34+
Ptosis and diplopia simultaneously as the initial indication.....	4	15+
Bilateral, simultaneous ptosis.....	1‡	4—
Ptosis of only one lid throughout the course of the disease.....	5	19+
Intermittent ptosis involving the two lids singly in an irregular alternation throughout the course of the disease.....	19§	73+

* One patient (patient 57) not included in this number had no double vision but had worn base-in prisms in her glasses for more than five years.

† One patient (patient 71) not included in this number had no ptosis but complained that her lids "felt heavy" periodically.

‡ The involvement was relatively severe, with troublesome diplopia, dysarthria and general muscular weakness of the extremities.

§ The ptosis of each patient varied in a most bizarre fashion from time to time and roughly paralleled the general systemic condition.

ocular or general. Repetition of movement induces fatigue at a speed that is almost pathognomonic of the disease. This symptom is most marked in the eyes, throat, mouth and neck, and relief is afforded only by rest. In addition, it has been observed that activity of one set of muscles may induce fatigue secondarily in muscles otherwise not showing signs of disability under normal conditions. Such fatigue was observed for example in patient 29, whose diplopia was always very marked after a day of what was, for her, heavy exertion.

Ocular manifestations, listed in the accompanying table, were considerably more common in our series than in series reported by previous investigators. (References to these investigators may be found in the

papers by Abraham,⁵ Rea,⁶ Sniderman,⁷ Viets and Schwab⁸ and Wilson.³)

DIPLOPIA

Diplopia is so variable a complaint that its classification is not possible except in a few cases of the most stable involvement, that is in cases in which the prognosis is the most favorable. It may be variable in any or all of the following factors: (a) amount as measured by ordinary methods, (b) the particular muscle or muscles involved and (c) the state of the disease at the time the patient was examined, i. e. whether it was in some phase of exacerbation or of recession or in complete remission.

ROUTINE OF THE EXAMINATION

In attempting to classify the motor anomalies on the basis of the divisions noted, a group of the patients were interviewed. Statistical histories were taken, and each patient was asked to return for an ophthalmic examination after abstaining from oral doses of prostigmine bromide long enough to be nearly on the point of collapse. The duration of abstinence thus varied from three hours in a case of very severe involvement to two days in a case of mild involvement.

On arrival the patient was examined as to wrinkling of the forehead and strength of the orbicularis muscles. Ptosis was measured while the lids were relaxed and again during a maximal effort to elevate them. The pupils were examined as to their reaction to light, direct, and consensual, and as to reaction in accommodation. Refraction with induced myopia without cycloplegia was then done, and the accommodative power was measured on Prince's rule. The muscles were checked with the Maddox rod, the prism and the cover test. Some were further tested with the Maddox tangent cross, the low transmission red filter (RG-8), our modification of the "dark red glass" of Bielschowsky, being used. After the examination the diagnostic injection of prostigmine methylsulfate with atropine was given and the routine was repeated. This diagnostic test was used after withdrawal of prostigmine bromide in an attempt to elicit the symptoms, which in some cases were "buried" under treatment.

5. Abraham, S. V.: *Myasthenia Gravis*, *Arch. Ophth.* **7**:700-719 (May) 1932.

6. Rea, R. L.: *Neuro-Ophthalmology*, St. Louis, C. V. Mosby Company, 1938, pp. 345-346.

7. Sniderman, H. R.: *External Ophthalmoplegia: A Case of Myasthenia Gravis*, *Am. J. Ophth.* **23**:1035-1037 (Sept.) 1940.

8. Viets, H. R., and Schwab, R. S.: *The Diagnosis and Treatment of Myasthenia Gravis*, *J. A. M. A.* **113**:559-562 (Aug. 12) 1939.

MUSCULATURE ABOUT THE EYES

The power to wrinkle the forehead and the strength of the orbicularis oculi muscle, as roughly determined by the ability of the patient to elevate the supercilia and close the eyelids against the resistance of the examiner's fingers, paralleled the ptosis in most cases. In some isolated cases there was "fair" to "good" forehead-wrinkling power in the presence of marked ptosis. The smooth face with the "myasthenic snarl" on smiling, as described by Wilson,³ was observed in some of the cases of more severe myasthenia in which there was considerable involvement of the facial muscles. Some patients in whom this facies is the most typical, as well as some patients with ptosis, are completely relieved of the complaint by the oral administration of prostigmine bromide and allied therapy. The majority of the patients are relieved somewhat by medication, although a few show but little improvement in the status of the facial involvement. It must be noted that in each patient there is an ebb and flow of the severity of these signs in relation to the amount of therapy and of physical exertion and to the stage of the disease at the time of observation.

Ptosis when it occurred was measured with an ordinary pocket rule in millimeters of vertical palpebral aperture between the lower corneal margin of the upper lid and the upper corneal margin of the lower lid. In the normal, nonmyasthenic person with the eyes in the primary position and the gaze straight ahead the aperture is about 8 mm. in a normally illuminated room and can be extended by extreme voluntary elevation to about 12 mm. In myasthenic patients the palpebral aperture varies from almost complete closure to the normal width, the average patient with moderate involvement showing an opening of about 5 mm. which increases to perhaps 7 to 9 mm. on voluntary elevation accompanied by great effort. This status changes as the process is repeated, and after voluntary elevation a dozen or so times the patient's ptosis becomes worse in the position of primary gaze. Then any attempt at raising the lids usually succeeds only in increasing the ptosis in this position and at best produces only a slight lifting of the lids. The strength of the orbicularis muscle also fails rapidly after repeated "squeezing" of the lids, this weakening being brought about sooner if the examiner opposes the action with his fingers.

ACCOMMODATIVE POWER

Refraction was done on such patients as could safely go without therapy, because, although difficulty in convergence has been noted in the literature for a long time, the status of accommodative power has not been specially mentioned. All the patients were questioned as to their ability to read clearly at near range. One patient, a woman in

whom the condition was mild, complained that reading was difficult, but after withdrawal of prostigmine refraction gave the following results:

Vision in the right eye was 6/9 uncorrected and 6/6 with a correction of $+1.50$ sph. $\ominus -0.37$ D. cyl. axis 75, and that in the left eye was 6/6 both uncorrected and with a correction of $+1.25$ D. sph. $\ominus -0.75$ D. cyl. axis 40. Use of a pinhole aperture did not improve the vision. There was vertical orthophoria for distances of 33 cm. and 6 meters, with 3 prism diopters of esophoria for near and for distance vision. With correction there was 10 D. of accommodative power in each eye, which is well within the normal range for the patient's age (23 years). It was felt that she had questionable accommodative esophoria. Another patient in our series was seen at the Massachusetts Eye and Ear Infirmary by Dr. Julian Chisholm, who felt that she had accommodative insufficiency, but as she was highly apprehensive in regard to her condition and suffered from most distressing diplopia, he repeated the refraction and found that she too was normal in respect to accommodative power.

Of the other patients (some of whom wore appropriate presbyopic correction) only a few experienced discomfort caused by diplopia at any time on attempting to read fine type, and all could read the type. Refraction performed on 9 showed for each an accommodative power compatible with his age. In fact, if any one point stands out it is the finding that all showed a slightly higher amount of accommodative power (0.5 to 1 D.) than was to be expected. This observation might bear more careful study after a comparison of the results obtained by refraction performed with and without cycloplegia. One patient in this group had been for some time under the care of Dr. Mahlon Easton, who stated that he also showed normal accommodative power and no remarkable refractive error.

PATHOLOGIC PHYSIOLOGY OF THE EXTRAOCULAR MUSCLES

Attempts at measuring the diplopia and thereby discovering which individual muscles were involved were essentially fruitless when one observed the patients over a sufficiently long period, with numerous periodic examinations. It was found early in our studies that there was no consistency in the amount of involvement or in the identity of the muscle or muscles involved even in the individual patient when examinations were done at intervals over a period of from several months to a year and a half. The most consistently observed defect was convergence insufficiency. This finding was not unexpected, since this function of the extraocular muscles involves probably the most frequently used coordinated movement of the eyes of civilized man and in myasthenia gravis, which is characterized by muscular weakness accentuated by exertion, difficulties in convergence should therefore

appear with relatively great frequency. The most uncomfortable motor anomalies observed were the vertical phorias and those involving torsion of the images. Fortunately for the patients, these abnormalities were considerably less common than were the horizontal phorias. Diplopia roughly paralleled the severity of the other signs and symptoms.

Abraham⁵ reported 6 cases of myasthenia gravis in 1932 and described his examination of the vertical phorias by a method of alternately turning Risley prisms of steadily increasing power base up and base down and graphing the deviations produced. His figures show a typical myasthenic deviation and wavering of the amount of phoria similar to that which we have found, but in the light of present theories regarding the nature of myasthenia gravis his conclusion is a misinterpretation of the evidence. He stated that "the actual turning of the eye in the direction of the apex of the prism, indicating that the muscle stimulated does not 'tire,' permit[s] of but one interpretation, namely, that the muscle or muscles stimulated contracted, but failed to relax promptly or completely, remaining in a prolonged contraction state."

The following case is typical of our findings and will disprove this thesis, we believe.

Patient 26, a man aged 32, had average, mild involvement. In 1930 he consulted an ophthalmologist, complaining of diplopia. He was given a collyrium, and his condition was diagnosed "a cold in the eye." His symptoms were entirely ocular. In 1932 ptosis developed in the left eye, and it later became bilateral. It then became restricted to the right eye, where it remained after 1934, when he entered the outpatient department of the Massachusetts Eye and Ear Infirmary and was referred to the Myasthenia Gravis Clinic. Both eyes had been grossly squinting in an irregular fashion since the onset of his disease. When I first saw him, in April 1940, there was exotropia, the right eye turning out about 10 degrees. He never had any difficulty (except diplopia) on near vision. The pupillary reactions were normal, and examination of the fundi, the external portions of the globe and the intraocular tension revealed no pathologic change.

After two days without prostigmine bromide he was examined. There were a fair amount of brow wrinkling, expressiveness of the face and a good smile. The right palpebral aperture measured 8 mm. and the left 10 mm. The vision in both eyes was 6/9—, and refraction with induced myopia without cycloplegia revealed the following error: right eye, —0.37 D. cyl. axis 90; left eye, +0.25 D. sph. —0.25 D. cyl. axis 90. The corrected vision was 6/5— in both eyes. The accommodative power was 6.5 D. singly in each eye, which is about normal for the patient's age. There were about 1.5 prism diopters of hyperphoria for near and for distance vision on the right, but this value constantly drifted up and down from 1 to 2 prism diopters, tending to become greater as the patient stared at the images of the muscle light and the "red dot" produced by the dark red filter placed over the right eye. When the horizontal phoria for distance was measured, the RG-8 glass being used in front of the right eye, the patient stated that he saw the red light far over to his left. When a 10 diopter prism base in was placed over the right eye he noted that the two images approached closely. A few seconds later he said that the red light had drifted back over toward the

left. A 12 diopter prism base in was put on, and again the two lights approached and drifted apart. The procedure was repeated with a 15 diopter prism, and at this point approximate coincidence of the images was obtained, but only for a minute or so, after which the red image crossed over to the right of the white light. It was then necessary to reduce the prism power to 14 and then to 12 diopters; approximation was again almost reached, but the red image once more passed the white light, to move out even farther to the left than when it was first seen. In this position it oscillated slowly, with occasional jumps toward the white light. This unusual sequence of events took place when the horizontal phoria for near range was measured, except that the sequence of base-in prisms (in prism diopters) was 6, 8, 10, 12, 10, etc.

This whole phenomenon, which I shall call the "drifting phoria" of myasthenia gravis, was observed in all the patients so tested in whom the diplopia was gross enough to be measured. Other patients observed only "wavering" of the red and white images.

On examination of the image of a flashlight thrown on the patient's corneas it was seen that the eyes were at intervals very slowly and irregularly shifting in abduction and adduction; but as base-in prisms were introduced and the necessity for converging was reduced the eyes showed more tendency to converge.

Because of the shifting, impermanent nature of this phenomenon, I have termed it the "transient tropia" of myasthenia gravis. It was demonstrable to a greater or lesser degree in all of our myasthenic patients in whom a frank tropia was observed.

These phenomena are not limited to the horizontal verging muscles but may be noted in any field of action in which a myasthenic muscle or group of muscles should function. We interpret in the following manner the phenomenon of the drifting phoria in this typical case: The patient suffers from "convergence fatigue," and when the correcting prisms are added in the first, or "supported relaxation," phase the convergence mechanism is relieved of part of its load; but in the constant voluntary attempt to close the slight gap between the lights and thus align them the mechanism becomes more fatigued and consequently permits the eyes to drift farther laterally. This struggle, repeated again and again, continues until prism overcorrection by the examiner has taken place, at which point there is no stimulus to convergence because the images are in alinement. After a short resting period the convergence block, or whatever the fault is, subsides, reversal of the images is reduced and a reduction of prism power is called for. This is the brief "reversal phase." Shortly afterward the convergence mechanism again becomes weakened, the lights shifting once more into the position of the first phase, and again an increase in the original corrective prism is called for. This two phase stage of the phenomenon (depending on the severity of the involvement) swings back and forth over a moderate range several times and then settles down into a third, very long phase

of short oscillations of the images well out in the field of the tropia, with occasional reversals of the process into the second phase. In cases of very severe involvement this phenomenon may not appear because the myasthenia is more like an ophthalmoplegia.

This extraocular muscle phenomenon can be likened to the antics of that member of the family Hydrobatidae, the water strider, who scurries out into a swift-moving brook and darts furiously upstream, becomes fatigued and is carried down, darts up and floats down, until he is reduced to sporadic spurts and then is compelled to float with the stream or regain land. Myasthenic patients are forced to go down with the stream until they reach some therapeutic shore or have a remission.

I have described the typical myasthenic "transient tropia" and "drifting phoria." Referring back to patient 26 who was left with vision corrected but in the grip of the horrid diplopia: He is thrown a life preserver — prostigmine. This parasympathomimetic drug was first introduced in the treatment of myasthenia in 1934 by an English ophthalmologist, Dr. Mary B. Walker.^{8a} She reasoned that myasthenia gravis, which symptomatically resembles curare poisoning, might be benefited by the administration of prostigmine, which is closely akin pharmacologically to physostigmine, a well known antagonist to the action of curare. There is no explanation of the action of prostigmine in myasthenia. It has been suggested that this drug acts either by interfering with the action of the overabundance of acetylcholine esterase, when this is credited with causing the myasthenia, or by supplementing the action of acetylcholine, when a deficiency in this substance is held to be the cause of the disease.

PROSTIGMINE METHYLSULFATE TEST

Prostigmine methylsulfate⁹ for the diagnostic test is available for intramuscular or subcutaneous injection in ampules containing 1.5 mg. ($\frac{1}{40}$ grain) of prostigmine methylsulfate and 0.6 mg. ($\frac{1}{100}$ grain) of atropine sulfate in sterile water. The atropine is included to overcome or to modify the abdominal discomfort caused by the parasympathetic-stimulating effect of prostigmine on the intestines. This ampule was introduced by Schwab and Viets^{9a} in 1938.

The patients are allowed a short rest after the "ordeal by prisms," and then an ampule of the prostigmine methylsulfate solution is injected.

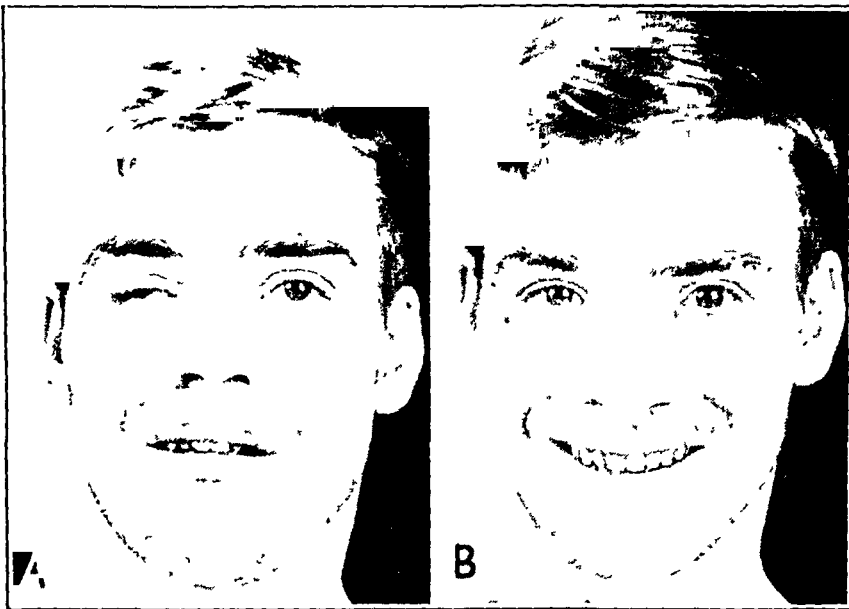
8a. Walker, M. B.: Treatment of Myasthenia Gravis with Prostigmine, *Lancet* 1:1200 (June 2) 1934.

9. Prostigmine methylsulfate, manufactured as "diagnostic ampules prostigmine methylsulphate with atropine" by Hoffmann-La Roche, Inc., who supplied it for these studies.

9a. Schwab, R. S., and Viets, H. R.: The Prostigmin Test in Myasthenia Gravis: Third Report, *New England J. Med.* 219:226-228 (Aug. 18) 1938.

Fifteen to twenty minutes is allowed for the drug to take effect, as it has been found in the general neurologic use of this medication that patients should show an improvement by the end of this time.

After injection, the facial expression of patient 26 was good, the ptosis of the right eye had disappeared and on elevation of the lids against resistance the strength of the levator palpebrarum muscle was excellent in both eyes. With voluntary elevation of the lids the palpebral aperture measured 11 mm. vertically in the right eye and 12 mm. in the left. The pupils reacted normally to light, direct and consensual. They constricted in accommodation for a near object, and the converging power was good. The eyes appeared to be grossly straight. On refraction the patient accepted a correction for the right eye of -0.25 D. cyl. axis 90 and for the left eye of $+0.25$ D. sph. $\ominus -0.25$ D. cyl. axis 90. The visual acuity was 6/5 — in both eyes. The patient was found to have 2.5 prism diopters of



A, patient 26 when requested to open his eyes as broadly and to smile as widely as possible before the diagnostic intramuscular injection of prostigmine methylsulfate with atropine sulfate. Exotropia of the right eye is well marked. The "myasthenic snarl" is barely visible on the right side of the face. *B*, fifteen minutes after the diagnostic injection.

hyperphoria on the right for both near and distance vision without any wavering of the images. He was 5 prism diopters esophoric for distance vision (perception of muscle light at 6 meters) and 1 prism diopter esophoric at a distance of 33 cm. There was no horizontal wavering of the images. The accommodative power was 6.5 D. in each eye tested singly. Subjectively, the diplopia was gone.

Other patients had diplopia in various fields, as well as the drifting phenomenon. They were relieved by the administration of prostigmine methylsulfate to a more or less equal degree, depending on the general response to therapy—which varies with the individual. In no case was there complete paralysis of any particular muscle or group of muscles supplied by any specific ocular cranial nerve.

The phenomenon of recurrent, multiple, variable, irregularly scattered ophthalmoplegias of one or more muscles is commonplace in myasthenia gravis. Sniderman recently described a case in which there were ptosis of both lids and paresis of both superior rectus muscles and of both medial rectus muscles, with the lateral rectus muscle of one eye also involved. The patient improved after the diagnostic injection of prostigmine methylsulfate and subsequently (symptomatically) with oral prostigmine bromide therapy, and in all respects the findings agree with ours.

PUPILLARY REACTIONS

The pupillary reflexes were essentially normal in our series, although in a few cases they were occasionally sluggish. This finding is in agreement with that by Wilson,³ who stated also that in his cases and in those of Markeloff, Boldt, Mendel and others the reactions to light and the response in convergence were enfeebled on sufficient repetition of the stimulus. We did not find this to be so in our cases except in one of recent involvement (not included in the series because of insufficient examination), in which there was progressive diminution of the reactions on repeated stimulation but not total abolition of the reactions. Wilson quoted Rakonitz as reporting "that the myasthenic pupil, contracted by light, will not become still smaller on accommodation whereas when reduced in size by the latter it can be narrowed further by the former." We cannot confirm this statement, since in our cases of sluggishness—the only pupillary abnormality found—repetition of the tests yielded only equivocal results.

In 2 other cases in this series there were atypical pupillary reactions not associated with and probably not due to myasthenia gravis. Patient 58 had typical Argyll Robertson pupils with persistently negative Wassermann tests of the blood and of the cerebrospinal fluid; a thorough neurologic study in the Massachusetts General Hospital failed to account for the abnormality. Patient 29 complained of transient mydriasis without cycloplegia and stated that 3 prostigmine bromide tablets of 15 mg. ($\frac{1}{4}$ grain) each and 2 ephedrine sulfate tablets of 25 mg. ($\frac{3}{8}$ grain) each caused her pupils to constrict but that terrific abdominal cramps followed medication. During one "attack" of mydriasis I saw her and found the pupils to be of normal size. On one occasion, while she was in the hospital for other medical studies with prostigmine bromide withdrawn, she demonstrated a transient reverse near reaction (perverse pupillary reaction), i. e. mydriasis on accommodating for a near object, but the pupils gradually constricted as she continued to fix on the object for a few seconds. It was not an Adie pupillary reaction. Perhaps the mydriasis can be explained on the basis of stimulation of the sympathetic nervous system accompanying the apprehension and excitement experienced by all patients with "active" myasthenia when their medication is withdrawn.

In several normal, nonmyasthenic controls it was noted that dilatation of the pupils followed the diagnostic injection of prostigmine bromide. This reaction was duplicated in one of the controls by an injection of physiologic solution of sodium chloride. I think this phenomenon is caused by fear, pure and simple, although several patients complained that palpitation and a "fear of dying" followed the injection and one middle-aged man admitted that he was "deathly afraid for a few minutes" of defecating spontaneously. Ordinarily the atropine in the diagnostic ampule prevents any gastrointestinal side effects. In this discussion of controls it might be well to interpose mention that 2 patients with congenital ptosis and 1 with post-traumatic ptosis were not benefited by the diagnostic test.

I offer no explanation, but one wonders why the pupillary muscles and those of accommodation are not involved as much as the other muscles about the eyes.

A possible explanation has been offered by Dr. David Cogan:¹⁰

Acetylcholine has a twofold pharmacologic action, called by Cannon and Rosenblueth¹¹ the muscarine-like effect and the nicotine-like effect. The muscarine-like effect causes stimulation of the parasympathetically innervated organs at the myoneural junctions and may be completely abolished by atropine. The nicotine-like effect causes stimulation of all autonomic nerves at the interneuronal junction provided the drug is used in small doses and is unaffected by atropinization. It is presumably the latter effect which occurs at some myoneural junctions. The functions of extraocular muscles are peculiarly sensitive to or dependent on the acetylcholine mechanism (Duke-Elder¹²). Their sensitivity to acetylcholine is unlike that of any other skeletal muscle. It does not seem surprising, therefore, that a general disturbance in the utilization of acetylcholine should manifest itself first and most profoundly in the extraocular muscles.

This explanation, however, would indicate only that it is the nicotine-like effect which is hypoactive, and it provides no evidence of the state of activity of the muscarine-like effect. But the fact that the beneficial effects of prostigmine and of physostigmine in myasthenia gravis are not prevented by the simultaneous administration of atropine (as in the diagnostic ampule) is evidence that it is exclusively the nicotine-like action of acetylcholine which is lacking in this disease. The integrity of the muscarine-like effect is further borne out by the normal pupillary size and reactions in myasthenia gravis. As cholinesterase affects both actions of acetylcholine, the presence of normal pupils would also indicate that an increased activity of cholinesterase does not account for the disease, as has been suggested (Pritchard¹³).

10. Cogan, D. G.: Personal communication to the author from the Howe Laboratory of Ophthalmology, Harvard Medical School.

11. Cannon, W. B., and Rosenblueth, A.: *Autonomic Neuro-Effector Systems*, New York, The Macmillan Company, 1937.

12. Duke-Elder, W. S.: *New Observations of the Extraocular Muscles*, Tr. Ophth. Soc. U. Kingdom **50**:181-199, 1930.

13. Pritchard, E. A. B.: *The Use of Prostigmine in Myasthenia Gravis*, *Lancet* **1**:432-435 (Feb. 23) 1935.

What evidence is present in the eyes and in the extraocular muscles would indicate, therefore, that the manifestations of myasthenia gravis are attributable to a selective hypoactivity of the nicotine-like effect of acetylcholine and that the muscarine-like action of acetylcholine and the cholinesterase mechanism are apparently normal.

REFRACTION

The refractive errors found in the patients tested were not remarkable, resembling the run of the lot as found in the patients examined in any week (there were no children; the ages ranged from 19 to 56 years).

No patients, either voluntarily or on almost leading interrogation, reported symptoms of asthenopia which could be associated with the course of the disease.

Prostigmine has no effect on the visual acuity in myasthenia gravis, which disease does not appear to affect visual acuity.

THERAPY

Medical treatment of the myasthenic patient is a delicate therapeutic problem, too complex for the busy ophthalmologist, and the care of such a patient should be entrusted by preference to a neurologist or an internist.

Prostigmine methylsulfate is rapid in action, but its effect is of brief duration. The bromide salt is therefore more suitable for symptomatic maintenance therapy. Although it is slow in action when taken orally (emergency situations, such as the occurrence of diaphragmatic paralysis, demand the initial use of the injectable methylsulfate), by its use a patient may be more easily held at a satisfactory activity level.

Patients are regulated to the point of remission of the symptoms with from three to twenty-five (15 mg.) prostigmine bromide tablets a day. Frequently antimyasthenic drugs, such as potassium chloride, ephedrine sulfate and guanidine hydrochloride, are successfully used in conjunction with the rather expensive prostigmine bromide as effective substitutes for a portion of that drug.

While myasthenic patients are benefited by the use of prostigmine and by allied therapy, many patients though able to resume a relatively normal life complain bitterly of the intermittent diplopia with or without ptosis. These symptoms are most commonly associated with the late hours of the day, when generalized fatigue sets in, and the patients are not content unless the ophthalmologist can help them overcome their visual difficulties.

Ptotic lids can be held up when the need arises with a strip of gummed cellophane tape, the $\frac{1}{2}$ inch (1.3 cm.) width being procurable in most stationery stores. This suspension is transparent, is relatively

inconspicuous and is inexpensive. It can be removed with ease when the occasion of its use has passed. Any operative attempts to correct myasthenic ptosis are doomed to failure.

It is impossible to supply prismatic correction for the diplopia in myasthenia, as this double vision is constantly in a state of flux. We have found that some of our patients who wear glasses are satisfied with a simple black plastic clip-on occluder worn first over one eye and then over the other on alternate days. These patients are warned of the possible danger of loss of vision should one eye be covered continuously, although we know that amblyopia exanopsia is exceedingly rare after adolescence. Less conspicuous but not as efficient is the "streaked lacquer" type of occlusion; first one and then the other spectacle lens is brushed with lacquer so as to blur one of the diplopic images badly. Each lens in turn is cleaned with "remover" of the previous day's covering, so that one of the images is clear on alternate days. We have found that the most satisfactory lacquer of this type is "cutex polish foundation," a free-flowing uncolored, semiopaque liquid which produces a better fog, is less costly than regular ophthalmic occluding lacquer and is easily cleaned off with any regular nail polish remover yet will remain on the glass for weeks if it is washed only with soap and water. It can be bought by the patient in any drug or 5 and 10 cent store.

For the patient who does not wear spectacles an eye patch seems to be the only recourse during bouts of diplopia unless he chooses to wear dark glasses with the back of one lens covered. For this purpose we suggest a piece of light brown wrapping paper held in place with regular white library paste. This is the least conspicuous form of occlusion according to our younger female patients, for, as much as some ophthalmologists may deplore the fact, "sunglasses" are ubiquitous and even in the dead of winter are commonplace in the eyes of the public. The light brown paper as seen through the dark lens matches the color of the lid of the other eye as seen through its uncovered lens by the casual observer. These points may appear to be inconsequential, but if they contribute to the mental comfort as well as to the physical well-being of myasthenic patients, so many of whom are extremely sensitive about their condition (for, as one of them put it, "we are half well"), physicians must seize on even the trivial in the healing of the soul as well as of the body.

SUMMARY

Myasthenia gravis is briefly discussed as to current hypotheses regarding the causation, the incidence according to age and sex and the predisposing factors. Modifications of the course are noted.

The general symptomatology is discussed. The results, including tabulation, of a study of the types of ocular manifestations and of their frequency in our series, are given. The signs and symptoms are discussed individually: diplopia, effects on the ocular musculature, ptosis, pupillary reactions and accommodative power. A discussion of a typical case of myasthenia gravis and of the diagnostic use of prostigmine methylsulfate is included, with a consideration of the phenomena "transient tropia" and "drifting phoria."

The pupillary reactions of the myasthenic patient and of the normal person on the diagnostic injection of prostigmine methylsulfate are noted. The therapy of the ocular complaints is briefly discussed.

CONCLUSIONS

1. Ocular manifestations in myasthenia gravis are due not to a contracted state of the musculature involved but to some neuromotor dysfunction that is considerably benefited by the administration of prostigmine. Cogan¹⁰ suggested that there may be a selective hypoactivity of the nicotine-like effect of acetylcholine with an apparently normal muscarine-like action and cholinesterase mechanism.

2. The extraocular muscles in this disease commonly exhibit the phenomena of "transient tropia" and "drifting phoria," which are relieved by prostigmine in some cases.

3. The pupillary reactions are usually normal and appear to be unchanged by prostigmine therapy.

4. There are no remarkable refractive errors associated with myasthenia gravis, and no change in visual acuity has been found with or without therapy.

5. The accommodative power is usually normal and appears to be unchanged by therapy.

6. The ocular manifestations of myasthenia gravis are more common than is generally thought, and the ophthalmologist is afforded an excellent diagnostic aid in the form of intramuscular injections of prostigmine methylsulfate solution.

ETIOLOGY OF UVEITIS

A CLINICAL STUDY OF 562 CASES

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The significance attributed to the various systemic infections and diseases believed to cause endogenous uveitis varies enormously in different clinics, in different localities and in succeeding decades. These variations appear due to the individual bias of the observer, to the prevalence of certain diseases in certain localities and to the steady improvement in diagnosis and in medical knowledge.

Table 1 gives a summary of the more significant of the published reports on the etiology of uveitis and illustrates the changing opinion of ophthalmologists. In the middle of the last century uveitis was regarded as due to syphilis, rheumatism, gouty diathesis or tuberculosis. In the latter part of the century localized pyogenic infections were occasionally blamed.¹ In the early part of the present century, in the flush of popularity enjoyed by the doctrine of focal infection, uveitis was attributed to localized focal infections in an increasing number of cases in this country and in England. On the other hand, in Germany the tendency was to attribute uveitis in a greater number of cases to tuberculosis and to minimize the importance of focal infection. With the introduction of the Wassermann reaction it became clear that the importance of syphilis as an etiologic factor, especially in disease of the posterior part of the uvea, had been greatly overestimated. During the past fifty years the numbers of cases of uveitis attributed to syphilis have steadily decreased. Gonorrhea has maintained a small but definite place as a causative factor.

The study here reported was undertaken with the idea of making a statistical analysis of the causes of uveal disease as shown in the case histories of patients with iritis, cyclitis, choroiditis and generalized uveitis who were admitted to the wards of the Wilmer Ophthalmological

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Read before the Section on Ophthalmology at the Ninety-Second Annual Session of the American Medical Association, Cleveland, June 5, 1941.

1. Nettleship, E.: Roy. London Ophth. Hosp. Rep. 9:182, 1877.

TABLE 1.—*Examples of Published Statistics on the Causation of Uveitis*

Author	Number of Cases	Tubercu- losis, Per- centage	Syphilis, Per- centage	Gonorr- hea, Per- centage	Foci of "Rheuma- Pyogenic tism" Infection, Per- centage	Metabolic Disease, Per- centage	Other Causes, Per- centage	Cause Undetermined or Not Stated, Per- centage	Comments
Artl, C. F.: Die Krankheiten des Auges, ed. 5, Prague, F. A. Crehner, 1863, vol. 2, p. 80	152	36	17	22	..	26	
von Wecker, L., in Graefe, A., and Saemisch, E. T.: Handbuch der gesammten Augenheilkunde, Leipzig, Wilhelm Engelmann, 1876, vol. 4, p. 485	Not stated	..	60 to 70	30 to 40	Iritis only
Hutchinson, J.: Tr. Ophth. Soc. U. Kingdom 5:1, 1885.....	104	55 to 83	17 to 45	..	"Arthritic" Iritis only
Zentmayer, W. M.: Therap. Gaz. 31:521, 1907.....	Not stated	..	70	15	..	15	Iritis only
Leber, A.: Arch. f. Ophth. 73:1, 1929.....	142	25	29	46	
Hessberg, R.: Klin. Monatsbl. f. Augenh. (supp.) 48:60, 1910	70	7	27	37	..	29	
Butler, T. H.: Brit. M. J. 1:894, 1911.....	100	6	22	6	12	6	1	6	41
Lang, W.: Lancet 1:1368, 1913.....	383	7	20	5	51	..	9	8	..
Goulden, C.: Roy. London Ophth. Hosp. Rep. 19:328, 1914....	100	1	42	8	43	1	6
Irons, E. E., and Brown, E. V. L.: J. A. M. A. 81:1771 (Nov. 21) 1923	200	4	19	5	63	5	4
Bulson, A. E.: Tr. Am. Ophth. Soc. 23:292, 1925.....	100	..	33	5	58	2	Iritis only
Gilbert, W., in Schleck, F., and Brückner, A.: Kurzes Handbuch der Ophthalmologie, Berlin, Julius Springer, 1930, vol. 5, p. 3	500	46	17	3	3	3	1	11	Iritis only
Gilbert, p. 101.....	50	70	8	Choroiditis only
Gifford, S. R.: Am. J. Ophth. 14:100, 1931.....	118	9	17	7	49	..	2	..	Iritis only
Irons, E. E.: Am. J. Ophth. 14:1228, 1931.....	26	15 to 53	0 to 12	0 to 4	30 to 76	4	Iritis only (chronic)
Urbanek, J., and Meller, R.: Ztschr. f. Augenh. 77:17, 1932....	500+	90+	10—
Zeman, W. P. E., in Berens, C.: The Eye and Its Diseases, Philadelphia, W. B. Saunders Company, 1936, p. 634	290	40	10	12	No figures given	No Iritis only

Institute of the Johns Hopkins Hospital from the time it was opened in 1925 to the present. A preliminary survey of these histories revealed at once certain variations in the diagnostic survey employed during the period the material accumulated. These variations were due to changing opinion of the importance of certain possible factors and to the inclusion from time to time of additional diagnostic procedures. The most radical change in the diagnostic study occurred in 1939, when the importance of brucellosis and of sarcoid in the causation of uveitis was fully recognized and a special search for these diseases became routine. It was therefore decided to terminate the study as of June 30, 1939, it being fully realized that most cases of uveal disease due to brucellosis and probably some cases of uveal disease due to sarcoid had up to that time been erroneously classified. When sufficient material has accumulated to reflect the importance of brucellosis and of sarcoid in the causation of uveal disease a second statistical report will be made.

MATERIAL FOR STUDY

In this series only patients admitted to the wards of the hospital are included. Patients treated in the outpatient departments or in private offices of the institute are omitted because their records are frequently incomplete and inadequate for statistical study. A preliminary survey revealed that the mass of incomplete outpatient material was so overwhelming that it did not appear worth while to attempt to isolate the wheat from the chaff.

Many of the histories of patients with uveitis admitted to the hospital wards were likewise unsuitable for a statistical analysis. The reason for this was that a great number of patients had been admitted for some special diagnostic or therapeutic procedure and after it had been done were discharged without further diagnostic study. In all, from 1925 to June 30, 1939 approximately 1,500 patients with uveal disease were admitted to the wards of the Wilmer Institute. Of these, the histories of only 562 satisfied the criteria we believed necessary for a statistical diagnostic study. An analysis of these 562 case histories forms the basis of this report.

The 562 patients include every patient with acute or chronic endogenous uveal disease admitted to the hospital from 1925 to June 30, 1939 for whom an adequate survey for determination of the cause of the uveal inflammation was made. These patients either were admitted primarily for treatment and while in the hospital were studied for determination of the cause of the uveal disease or were admitted primarily for making of the diagnostic survey. The only histories excluded from the study were those of patients for whom, for one reason or another, a complete diagnostic survey was not made.

The fact that these patients were all admitted to the hospital, either for treatment or for study, indicates that as a general rule the uveal disease was probably more severe or obscure than in the average case. The relative severity of the uveal disease is shown in table 2, which illustrates the ocular complications and the extension of the uveal disease to other parts of the eye. Thus, of the patients with anterior uveal disease alone only 37 per cent were free of other ocular complications; of the patients with choroiditis alone 74 per cent were free, and of the patients with generalized uveitis only 35 per cent were free.

An attempt to differentiate between acute and chronic involvement proved most unsatisfactory, because often the uveal inflammation ran an acute course in one attack and a chronic course in another attack in the same patient. Considering only the first attack of inflammation and judging the course according to rather indefinite criteria, the disease

TABLE 2.—*Complications of Uveitis*

Complications	Anterior Uveitis Alone (210 Patients), Percentage	Posterior Uveitis Alone (154 Patients), Percentage	Generalized Uveitis (198 Patients), Percentage
Interstitial keratitis.....	16.7	0.7	12.1
Other corneal involvement.....	11.0	1.3	7.1
Scleritis.....	2.0	0.7	3.5
Definite neuroretinitis.....	1.0	2.6	2.5
Complicated cataract.....	18.1	9.7	30.8
Secondary glaucoma.....	33.3	4.5	32.3
Detachment of retina.....	2.0	11.7	9.6
Any of above.....	63.3	26.0	65.2

began as an acute condition in 33 per cent and as a chronic condition in 67 per cent. A history of previous attacks of ocular inflammation was obtained from 341 of these patients, i. e. from 56 per cent of the patients with anterior uveitis, from 72 per cent of the patients with posterior uveitis and from 61 per cent of the patients with generalized uveitis. Therefore, in a large proportion of the patients the uveal disease was either recurrent or chronic. A classification of the 562 patients according to the portion of the uveal tract involved and as to whether or not both eyes were involved (at any time, not necessarily simultaneously) is given in table 3. Table 4 gives the classification as to race and sex and table 5 the age distribution. A total of 327 patients were followed for more than one year.

Practically all the case histories used in this study contained as a minimum data on: 1. A complete examination of the eyes, including external, ophthalmoscopic, slit lamp, refraction and perimetric examination. 2. A general physical examination, with a complete medical history. 3. Routine laboratory examinations of the urine, hemocytologic study and study of the blood chemistry (when indicated, studies

of the renal function were made). 4. Serologic tests of the blood for syphilis. 5. Quantitative determination of the intracutaneous sensitivity to tuberculin with Koch's old tuberculin. 6. A routine search for foci of infection in the teeth, tonsils, accessory nasal sinuses and genito-urinary tract. In the few case histories which did not contain these minimum data—not over 50 in all—the diagnosis was perfectly clear

TABLE 3.—*Clinical Extent of Uveal Inflammation*

Portion of Uveal Tract Involved	Number of Patients		Total
	Bilateral Involvement	Unilateral Involvement	
Anterior (iritis or iridocyclitis).....	128	82	210
Posterior (choroiditis).....	107	47	154
Generalized (both iritis and choroiditis).....	100	98	198
Total.....	335	227	562

TABLE 4.—*Race and Sex Distribution*

Race	Male Patients	Female Patients	Total
White.....	269	203	472
Negro.....	43	47	90
Total.....	312	250	562

TABLE 5.—*Age Distribution*

Age, Years	Number of Patients
0-9.....	7
10-19.....	59
20-29.....	131
30-39.....	117
40-49.....	113
50-59.....	75
60-69.....	47
70-79.....	12
80-90.....	1
Total.....	562

from the data available. Most of these were histories of patients with obvious syphilis, with a positive Wassermann reaction, or of patients with tuberculosis for whom a final diagnosis was made on histologic examination of an enucleated eye.

Roentgenograms of the chest were made for 287 of the patients, and after 1935 the report of the roentgenologist contained a special note on the presence or absence of enlarged or calcified mediastinal and hilar glands. Complement fixation tests for gonococci were not performed prior to 1936 but were usually done thereafter. At the beginning of

the series, in 1925, the search for foci of infection included roentgenologic studies of the gastrointestinal tract and the gallbladder, but by 1934 it had become apparent that these studies were not of value in determining the cause of uveitis and they were thereafter omitted unless there was some special indication. Such special procedures as the making of roentgenograms of joints and of intravenous pyelograms, cystoscopic examinations and dextrose tolerance tests were done only when ordered by the consultant in the special field. Roentgenograms of the teeth and of the accessory nasal sinuses, likewise, were made only when there was some suspicion of periapical infection or of sinus disease on clinical examination by the dentist or the otolaryngologist. As a matter of fact, such roentgenograms were made for the majority of the patients and certainly in every instance in which there was a suspicion of focal infection on clinical examination. Routine serologic tests for brucellosis and biopsy of a lymph gland for sarcoid were not done until 1939.

METHOD OF STUDY

Each case history was carefully reviewed and the pertinent data transferred to a punch card. After all the data had been assembled in this manner the statistical results were tabulated by mechanical sorting of the cards. In every instance in which there was any uncertainty of the results the original history was reviewed with regard to the pertinent point and the results checked. The final diagnosis of the cause of the uveal inflammation was reached after an evaluation of all the available evidence, including not only the history and the results of the examination of the eyes, of the general physical examination and of various diagnostic and laboratory procedures, but the subsequent course of the uveitis and any available histologic observations.

Approximately two thirds of the patients in this series were public ward patients, all of whom were cared for under the direct supervision of the director of the Wilmer Institute. The remaining third were private patients, practically all having been in the service of the director of the institute, either the late Dr. William H. Wilmer or his successor (A. C. W.). There should have been, therefore, a rather constant uniformity in examination and in diagnosis, and the results should be free of error which might arise from differences of opinion among different observers.

The criteria on which a positive or a presumptive diagnosis of the cause of the uveitis was made are given in detail under the discussion of the individual etiologic factors.

RESULTS

The 562 patients in the series make up two general groups. The first group consists of 244 in whom the sum total of available evidence pointed so clearly to some definite etiologic factor that a definite diag-

nosis appeared justified. With the exception of those with uveitis attributed to foci of infection, with regard to which fulfilment of the most rigid criteria yields only presumptive evidence of the cause, and possibly of a few with uveitis which was attributed to tuberculosis but which may have been caused by brucellosis or sarcoid, the classification of the patients in this group is probably subject to small error. The second group consists of the remaining 314 patients, in whom the evidence was considered either too scanty or too inconclusive to permit more than a tentative diagnosis, often not more than a fair guess, of the cause of the uveitis. The results of etiologic analysis for group 1, for group 2 and for the series as a whole are shown in table 6.

TABLE 6.—*Etiologic Factor: Diagnosis, Either Definite or Presumptive, for 562 Patients with Uveitis (All Percentages Based on Entire Series of 562 Patients)*

Etiologic Factor	Group 1: 244 Patients with Definite Evidence of Etiologic Factor		Group 2: 318 Patients with Presumptive Evidence of Etiologic Factor		Total: 562 Patients	
	No. of Patients	Per- centage	No. of Patients	Per- centage	No. of Patients	Per- centage
Tuberculosis.....	132	23.5	147	26.1	279	49.7
Syphilis.....	45	8.0	14	2.5	59	10.5
Sarcoid.....	3	0.5	0	0.0	3	0.5
Brucellosis.....	1	0.2	1	0.2	2	0.4
Foci of infection.....	31	5.5	116	20.6	147	26.1
Gonorrhea.....	10	1.8	16	2.8	26	4.6
Nongranulomatous systemic disease..	14	2.5	19	3.4	33	5.9
Metabolic disease.....	0	0.0	3	0.5	3	0.5
Miscellaneous.....	8	1.4	2	0.4	10	1.8
Total.....	244	43.4	318	56.5	562	100.0

A comparison of groups 1 and 2, table 6, shows a close conformity in the figures for tuberculosis but a marked variation in those for syphilis and in those for focal infection. The reason for the discrepancy in the figures for the last two diseases is obvious. When syphilis is the factor responsible for uveitis its presence can usually be readily proved by the general picture and the Wassermann reaction; thus the greater number of syphilitic patients would naturally appear in group 1, in which the etiologic diagnosis is definite. When a focus of infection is the apparent cause of uveitis the causal relationship is extremely hard to prove and the greater number of patients would appear in group 2, in which the etiologic diagnosis is presumptive only. As will hereafter be pointed out, various foci of infection were extremely common, not only in the patients in this series but in a control group of patients without uveitis. In the absence of other factors to which the uveitis may be attributed, there is a natural tendency to designate as the cause any focus of infection which may be present.

In 44 patients the diseased eye was enucleated and studied histologically. The reason for enucleation was almost always the same, the eye being blind and painful and either phthisical or with secondary glaucoma. In 3 additional patients a bit of iris was excised at iridectomy. Therefore material from 47 eyes was available for histologic examination. In this examination an effort was made to establish the etiologic factor responsible for the uveitis. Practically, this presented considerable difficulty.

From both the clinical and the histologic viewpoint uveitis may be classified as granulomatous or nongranulomatous. Clinically the granulomatous lesions are characterized by chronicity, by only a slight exudative reaction and often by the formation of visible nodules or tubercles; the nongranulomatous lesions are characterized by the absence of nodules, by a more acute inflammatory reaction (which may, however, become chronic and recurrent) and by exudation either of the "serous" or of the "plastic" type. Histologically the granulomatous lesions are characterized not only by the formation of tubercles but by destruction of tissue and its replacement by connective tissue, while the nongranulomatous lesions are characterized chiefly by cellular infiltration and exudation, with little destruction of tissue or overgrowth of connective tissue.

The most characteristic histologic lesions are those produced by the infectious granulomas, the most important of which are tuberculosis, syphilis, sarcoid, brucellosis, lymphogranuloma venereum and certain rather rare fungous infections. The histologic differentiation among these diseases, however, is none too clearcut, especially when the acute inflammatory phase is subsiding. Indeed, in the atrophic stage, in blind, phthisical eyes, the infectious granulomas leave few if any characteristic lesions. Serial sections are frequently necessary to demonstrate tuberculous lesions even in the presence of active inflammation, and when tubercles are found in the absence of stainable bacilli the lesions cannot be differentiated with certainty from the lesions of sarcoid or of brucellosis. In this series bacilli were demonstrable in only 2 of the 17 eyes which showed typical tubercles, but failure to find tubercle bacilli in sections from an area of known tuberculous inflammation is the rule rather than the exception. A clearcut classification from the etiologic viewpoint was therefore often impossible. Table 7 shows the pathologic diagnosis classified as far as possible from the etiologic viewpoint for the 47 patients from whom uveal tissue was available for histologic study.

Small as is the series of histologically examined eyes, nevertheless there is a striking similarity between the percentage of histologic diagnoses and the percentage of clinical diagnoses of syphilis and of tuber-

culosis. The uveitis of 4 eyes was ascribed to syphilis on histologic examination, a percentage of 8.3, as against a percentage for clinical diagnoses of 10.5. The uveitis in 36 per cent of the histologically examined eyes was diagnosed as tuberculous, as against a percentage for clinical diagnoses of tuberculosis of 49.7. In some of the histologically examined eyes which showed either nonspecific inflammatory lesions or old scarring (inactive uveitis, in which no characteristic lesions could be expected) the uveitis may well have been due to tuberculosis. If this could be established the percentage of histologically examined eyes with uveitis ascribed to tuberculosis would even more closely approximate the percentage of those with tuberculosis diagnosed clinically.

Cultures and animal inoculations of aqueous or excised iris tissue have proved uniformly fruitless as means of diagnosis in the experience

TABLE 7.—*Histopathologic Diagnosis of Condition in 47 Eyes **

Etiologic Factor	Tuber- culosis	Syphilis	Granu- lomatous Uveitis, Prob- ably Syphilis	Sarcoid	Uveitis Inactive; No Charac- teristic Lesion	Non- specific Inflam- matory Lesions	Total
Number of eyes.....	17	3	1	1	11	14	47
Percentage of those examined histologically.....	36	6	2	2	23	30	100

* The histologic examinations and pathologic diagnoses were made by Dr. Jonas S. Friedenwald.

of almost all investigators. Similar agencies were likewise fruitless in a few instances in the present series.

COMMENT: CRITERIA FOR ETIOLOGIC CLASSIFICATION

The criteria for attributing uveal inflammation in a given case to any of the various etiologic factors were as follows:

1. *Tuberculosis*.—The criteria adopted for a positive diagnosis of ocular tuberculosis (132 cases) and the number of patients in each of the various subgroups were as follows: 1. A histologic diagnosis of tuberculosis in the enucleated eye—17. 2. The occurrence in the eye of a focal reaction following the therapeutic use of tuberculin when a presumptive diagnosis of ocular tuberculosis was justified because of the clinical picture, the course of the condition and the diagnostic survey—18. 3. The development of so-called characteristic nodular lesions (either iris nodules or Koeppe nodules) without evidence of syphilis, sarcoid or brucellosis—22. 4. The development of associated retinal perivasculitis, deep scleritis, sclerokeratitis or interstitial keratitis when syphilis could be definitely excluded and the uveitis ran a course

and showed clinical findings consistent with tuberculosis—15. 5. A pronounced tendency of the uveitis to chronicity and recurrence, with mutton fat deposits on the posterior surface of the cornea if there was anterior involvement, in a patient with evidence of healed or active systemic tuberculosis or with a sensitivity to 0.001 or 0.01 mg. of old tuberculin injected intracutaneously, all other known etiologic factors having been excluded—60.

The criteria adopted for a presumptive or probable diagnosis of tuberculosis were as follows: 1. The occurrence of so-called characteristic iris nodules or Koeppe nodules in an eye with a general picture suggestive of tuberculosis but in a patient in whom the possibility of other infectious granulomas could not be excluded. 2. Evidence of healed or active systemic tuberculosis, a high degree of hypersensitivity to tuberculin or a course and clinical appearance of the ocular lesion suggestive of tuberculosis in a patient with no evidence of another causative factor. 3. Evidence of systemic tuberculosis or a high sensitivity to tuberculin in a patient with evidence also of either syphilis or foci of infection but with a clinical course characterized by chronicity and recurrences or with other lesions suggestive of tuberculosis (sub-group 4, group 1) and no evident relationship of the ocular disease to either foci of infection or syphilis.

In these criteria laid down for a positive and for a presumptive diagnosis of ocular tuberculosis the clinical picture and the course of the ocular lesion have been emphasized. In previous publications one of us (A. C. W.)² described both the so-called characteristic and the non-characteristic lesions of ocular tuberculosis. The characteristic lesions are nodular lesions with visible tubercles, Koeppe nodules or sweeping destructive lesions characterized by caseation and necrosis. The non-characteristic lesions are those lesions which frequently tend to become circumscribed, to heal and later recur or to run a chronic course with exacerbations and remissions. The pathogenesis of these lesions has likewise been described, with the roles that the virulence and the number of the infecting organisms, the amount of immunity and the degree of local hypersensitivity to tuberculin play in their causation. Experimental work has been presented to support the views.³ The significance of Koeppe nodules has been emphasized. These invariably indicate an epithelioid cell response and are therefore pathognomonic of infectious

2. Woods, A. C., and Randolph, M. E.: Treatment of Ocular Tuberculosis, *Arch. Ophth.* **18**:510 (Oct.) 1937. Woods, A. C.: *Am. J. Ophth.* **21**:366, 1938.

3. Woods, A. C.; Burky, E. L., and Friedenwald, J. S.: Experimental Studies of Ocular Tuberculosis, *Arch. Ophth.* **19**:229, 236 and 245 (Feb.) 1938; **23**:351 (Feb.) 1940. Woods, A. C., and Burky, E. L.: Experimental Studies of Ocular Tuberculosis, *ibid.* **23**:363 (Feb.) 1940; **25**:62 (Jan.) 1941.

granulomas. While Koeppe nodules may occasionally occur in non-tuberculous uveitis, in the vast majority of instances they are the result of tuberculosis.

The present study has shown that the type of keratitic deposits occurring in the course of uveitis is of some diagnostic significance. It has long been recognized that polymorphonuclear leukocytes agglutinate poorly and tend to settle on the posterior surface of the cornea as discrete cells while lymphocytes agglutinate more readily and form small but discrete keratic precipitates. Epithelioid cells agglutinate still more readily and tend to settle out as lardaceous or mutton fat deposits. Granulomatous lesions are made up predominantly of lymphocytes and epithelioid cells, while the acute sudden inflammatory reactions with dense fibrinous exudates are characterized chiefly by polymorphonuclear cells and later by lymphocytes. Tuberculous lesions should therefore theoretically be characterized by mutton fat (epithelioid cell) or discrete (lymphocytic) deposits on the posterior part of the cornea, while non-tuberculous or nongranulomatous lesions should show predominantly fine dustlike keratitic deposits of polymorphonuclear cells or small discrete lymphocytic deposits. An analysis of the types of keratitic deposits occurring in the patients of this series who showed active anterior ocular inflammation bears out this hypothesis. The keratitic deposits occurring in eyes with iris nodules and Koeppe nodules were either heavy mutton fat or discrete lymphocytic deposits in 95 per cent, while in only 5 per cent were they fine cellular keratitic deposits. On the other hand, 50 per cent of the eyes with acute inflammation and visible fibrin in the aqueous (rarely tuberculous in origin) showed fine cellular deposits, 31 per cent showed small discrete lymphocytic deposits and only 19 per cent showed mutton fat deposits. This finding lends support to the view that mutton fat deposits are usually indicative either of ocular tuberculosis or at least of a deep granulomatous lesion while discrete lymphocytic deposits may occur in either granulomatous or nongranulomatous uveitis.

It will be noted that in the criteria for a diagnosis of the tuberculous origin of a uveal lesion little stress has been laid on hypersensitivity to tuberculin. Of the patients whose uveitis was diagnosed as definitely tuberculous (group 1), only in the fifth subgroup was any particular attention paid to the reaction to tuberculin. This subgroup consisted of patients with a tendency to chronicity or recurrence, with mutton fat keratitic precipitates (if there was anterior inflammation) and with no evidence of any other possible etiologic factor. In these patients either evidence of systemic tuberculosis or a high degree of hypersensitivity to tuberculin was demanded to indicate the tuberculous origin. Similarly, for a tentative diagnosis of tuberculous uveitis (group 2), hypersensitivity to tuberculin was regarded as affording only slight corroborative evidence in the etiologic classification.

This skepticism over the clinical significance of either a positive or a negative reaction to tuberculin is in direct opposition to the older view that an active tuberculous focus anywhere in the body always produces a high degree of cutaneous sensitivity and that a low degree or an absence of cutaneous sensitivity is definite evidence that a suspected inflammatory focus is not tuberculous. The present lack of confidence in the reaction to tuberculin is supported by modern experimental work, which indicates that the antigenic stimulus from a tuberculous focus in the eye is insufficient to influence to any appreciable degree the cutaneous reactivity to tuberculin. However, as shown in table 8, if there are other indications that the ocular lesion is tuberculous a high degree of cutaneous reactivity to tuberculin does enhance the probability of a positive diagnosis of tuberculosis. In this table are shown the reactions to tuberculin of all the patients in groups 1 and 2 whose uveitis was diagnosed (definitely or presumptively) as tuberculous. In contrast are shown the reactions to tuberculin of the remaining patients in

TABLE 8.—*Intracutaneous Reactivity to Tuberculin of Patients with Tuberculous and with Nontuberculous Uveitis*

Type of Uveitis	No. of Patients	Reaction to 0.001 Mg. Positive	Reaction to 0.01 Mg. Positive	Reaction to 0.1 Mg. Positive	Reaction to 1.0 Mg. Positive	Patient Insensitive as Far as Test Was Carried
Tuberculous.....	270	43%	34%	14%	5%	6%
Nontuberculous.....	249	11%	29%	29%	7%	23%

the series, whose uveitis was diagnosed as nontuberculous. The greater degree of sensitivity to tuberculin of the tuberculous patients is manifest. Thus 43 per cent of these showed extremely high sensitivity, with a reaction to 0.001 mg. of tuberculin injected intracutaneously, while only 11 per cent of the nontuberculous patients showed this degree of reactivity. Likewise, only 6 per cent of the tuberculous patients were insensitive as far as the test was carried, while of the nontuberculous patients 23 per cent were insensitive.

The figures given in table 8 are open to the criticism that in some instances the high degree of sensitivity to tuberculin shown by the patient was a deciding factor in classifying the uveitis as tuberculous. To answer such a possible criticism a further analysis of the figures was made. From group 1 there were selected 67 patients for whom a positive diagnosis of tuberculosis had been made without regard to the reaction to tuberculin. Also, 14 patients with a histologic diagnosis of tuberculous uveitis and a known sensitivity to tuberculin were selected.⁴

4. The reactions to tuberculin of 3 patients for whom a histologic diagnosis was made are not known, the patients having been admitted to the hospital for the enucleation of blind phthisical eyes and no studies of the sensitivity to tuberculin having been made.

These two groups of almost undoubtedly tuberculous patients showed the same relatively high degree of hypersensitivity to tuberculin. The similarity of their hypersensitivity to tuberculin to that shown by the total group of definitely and probably tuberculous patients lends support to the probable accuracy of the diagnoses in the latter group. However, while these figures illustrate the tendency to a high cutaneous sensitivity to tuberculin in patients with tuberculous uveitis, they show clearly that with any individual patient little reliance can be placed either on a positive or on a negative reaction as a diagnostic aid. The margin of error is too great.

The demonstration of a systemic tuberculous focus from which the eyes might become infected is usually accepted as a criterion which enhances a probable diagnosis. The diagnostic value of such a demonstration is, however, somewhat problematic. It is generally conceded that the infecting bacilli are conveyed to the eyes by the blood stream

TABLE 9.—*Intracutaneous Reactivity to Tuberculin of Patients with Definitely Diagnosed Tuberculous Uveitis*

Type of Uveitis	No. of Patients	Reaction to 0.001 Mg. Positive	Reaction to 0.01 Mg. Positive	Reaction to 0.1 Mg. Positive	Reaction to 1.0 Mg. Positive	Patient Insensitive as Far as Test Was Carried
A.....	67	55%	28%	8%	6%	4%
B.....	14	36%	21%	21%	0%	21%

A. Patients whose clinical diagnosis was made without regard to sensitivity to tuberculin (criteria 1, 2, 3 or 4) as listed in text.

B. Patients with a histologic diagnosis and a record of sensitivity to tuberculin.

from a tuberculous focus elsewhere in the body and that the most frequent focus is in the mediastinal and the hilar glands. It is also recognized that ocular tuberculosis usually occurs in otherwise fairly robust and healthy persons and not often in patients with advanced pulmonary tuberculosis. It is obvious that the clinical demonstration of a small primary tuberculous focus may be somewhat difficult. However, according to most German reports roentgenologic study of the chest or physical examination discloses evidence of systemic tuberculosis in from 70 to 100 per cent of all patients with ocular tuberculosis.⁵ Our figures are not so conclusive.

Prior to 1935 roentgenograms of the chest were not taken as a routine in the study of the causation of uveal disease and no special notes were made on the presence or absence of enlarged or calcified hilar glands, only casual mention of them being occasionally made. There are 97 patients with definite or probable tuberculous uveitis for whom roentgenograms of the chest were made prior to this date. The

5. Werdenberg, E.: *Klin. Monatsbl. f. Augenh.* (supp.) **94**:3, 1935. Grönholm, V.: *Acta ophth.* **6**:297, 1928.

data on these patients are shown in table 10. Irrespective of the presence or absence of systemic tuberculosis, there appeared no doubt as to the tuberculous nature of the ocular lesion in 25. The results of the roentgen examination of these 25 patients are likewise shown in table 10. In these two groups only 26 per cent and 36 per cent respectively showed evidences of pulmonary or mediastinal changes, this difference being of no statistical significance.

Beginning in 1935, roentgenograms of the chest were made routine in the diagnostic study of patients with uveitis and the roentgenologist

TABLE 10.—*Conditions Revealed by Roentgenograms of the Chest in Patients with Tuberculous Uveitis Prior to 1935*

Diagnosis	No. of Patients	Active Pulmonary Tuberculosis	Inactive Pulmonary Tuberculosis	Calcified or Enlarged Hilar Glands	Roentgenogram of Chest Negative for Tuberculosis
Definite or probable tuberculous uveitis.....	97	2%	12%	11%	74%
Made without regard to roentgenogram of chest * (selected patients).....	23	4%	20%	12%	64%

* Satisfying criteria 1, 2, 3 or 4 for a definite diagnosis as presented in the text.

TABLE 11.—*Conditions Revealed by Roentgenograms of the Chest in Patients with Tuberculous Uveitis After 1938*

Diagnosis	No. of Patients	Active Pulmonary Tuberculosis	Inactive Pulmonary Tuberculosis	Calcified or Enlarged Hilar Glands	Roentgenogram of Chest Negative for Tuberculosis
Definite or probable tuberculous uveitis.....	72	3%	11%	32%	54%
Made without regard to roentgenogram of chest * (selected patients).....	20	10%	15%	35%	40%

* Satisfying criteria 1, 2, 3 or 4 for a definite diagnosis as presented in the text.

was requested to make a special note on the presence or absence of any evidence of old hilar changes. There are available for analysis 72 such roentgenograms of patients with definite or probable tuberculous uveitis. The occurrence of tuberculous lesions in the chest and in the mediastinum in these patients is shown in table 11. Twenty of the 72 patients showed ocular and general evidence so clearcut that there was no doubt of the diagnosis of tuberculosis, regardless of the presence or absence of systemic infection. The data on these 20 patients are also shown in table 11. With the more careful roentgenologic study the percentage of demonstrable systemic tuberculosis rises for the general group with tuberculous uveitis to 46 per cent and for the group with undoubted tuberculous uveitis to 60 per cent, more closely approximating the lower of the German figures.

In summary, these statistical studies on the incidence of hypersensitivity to tuberculin and of systemic tuberculosis in patients with ocular tuberculosis indicate that the demonstration of a high cutaneous sensitivity to tuberculin or the demonstration of an active or healed systemic tuberculous focus enhances the probability that the diagnosis of ocular tuberculosis is correct, but they indicate that a low sensitivity, an absence of sensitivity or a negative roentgenogram of the chest is only slight evidence against such a diagnosis. An accurate diagnosis of uveal tuberculosis cannot be made for any patient merely because of a positive roentgenogram of the chest or a strongly positive reaction to tuberculin but must depend also on the clinical appearance and course of the inflammation and the exclusion of other possible factors.

The accuracy of a diagnosis of tuberculous uveitis is not greatly enhanced by response to therapy, since no therapeutic agent at present available will eradicate tubercle bacilli from the body. Gold salts have long been known to have a bacteriostatic or bactericidal effect in vitro on tubercle bacilli,⁶ but clinical results with gold preparations have at best been highly questionable.⁷ Sulfanilamide exerts a favorable effect on the course of tuberculosis in guinea pigs and in rabbits,⁸ but neither it nor related drugs have as yet been found of value in the treatment of either systemic or ocular tuberculosis in human beings.⁹ The value of trimethyldioxyoxotritan (rubrophen), a drug widely used of late in the treatment of extrapulmonary tuberculosis in Europe,¹⁰ is also questionable. Tuberculin therapy has long been thought to have a favorable effect on ocular tuberculosis by many, if not most, ophthalmologists. Adequate statistical proof of this contention is lacking because of the practical difficulty of obtaining a satisfactory control series, but in all probability it is correct. In the present series the general impression was gained that patients with ocular tuberculosis did better while taking tuberculin and that therapy over a period of years was more efficacious than a short course of treatment. The effect of tuberculin is not an

6. Koch, R.: *Deutsche med. Wchnschr.* **16**:756, 1890. Feldt, A.: *ibid.* **39**:549, 1913.

7. Schnaudigel, O.: *Klin. Monatsbl. f. Augenh.* **59**:353, 1917. Lundsgaard, K. K. K.: *Zentralbl. f. d. ges. Ophth.* **17**:637, 1927. Calmette, A.; Boquet, A., and Negre, L.: *Rev. de la tuberc.* **7**:169, 1926. Benedict, W. L., and Goeckerman, W. H.: *Foreign Proteins and Gold in the Treatment of Uveitis*, Tr. Sect. Ophth., A. M. A., 1932, p. 237. Remelé: *Zentralbl. f. d. ges. Ophth.* **43**:215, 1939.

8. Rich, A. R., and Follis, R. H., Jr.: *Bull. Johns Hopkins Hosp.* **62**:77, 1938. Follis, R. H., Jr., and Rich, A. R.: *ibid.* **65**:466, 1939.

9. (a) Faniel, H.; Jeurissen, A.; Courtois, R., and Dwelshauvers, F.: *Bruxelles-méd.* **19**:725, 1939. (b) Allison, S. T., and Myers, R.: *Treatment of Pulmonary Tuberculosis with Sulfapyridine*, J. A. M. A. **113**:1631 (Oct. 28) 1939. (c) Guyton, J. S.: *Am. J. Ophth.* **22**:833, 1939.

10. Licsko, A., and Hinterleitner, K.: *Zentralbl. f. d. ges. Ophth.* **40**:19, 1937. Raab, C. M.: *Ophthalmologica* **100**:1, 1940.

immediate one, however, being almost certainly dependent on a gradual reduction of ocular sensitivity. That subcutaneous tuberculin therapy does reduce cutaneous sensitivity in the majority of instances, and therefore presumably local ocular sensitivity also, is clearly shown in table 12. This table also demonstrates, however, that desensitization is a slow process and cannot be accomplished in every patient. The response to tuberculin therapy is therefore of limited value in establishing an etiologic diagnosis for any individual patient. Table 13 gives for 70 patients in this series with definite tuberculous uveitis the results of prolonged tuberculin therapy expressed in terms of focal reactions, recurrences and status of the uveitis when last seen. While these results are entirely

TABLE 12.—*Effect of Subcutaneous Tuberculin Therapy on Intracutaneous Sensitivity to Tuberculin*

Duration of Tuberculin Therapy	Number of Patients	Effect on Cutaneous Sensitivity to Tuberculin		
		Decrease	No Change	Increase
1 to 2 years.....	9	44%	44%	11%
Over 2 years.....	26	65%	27%	8%
Total.....	35	60%	31%	9%

TABLE 13.—*Results of Subcutaneous Tuberculin Therapy in Patients with Definitely Tuberculous Uveitis Who Were Treated More Than One Year*

No. of Patients	Average Period Followed	Focal Reactions	Recurrences of Uveitis	Final Status			
				Healed	Improved	Unimproved	Lost One Eye in First Attack
70	4.3 years	29%	34%	71%	21%	6%	1%

irrelevant to the present discussion and there is no adequate control group, they are included because the results may prove of value for comparison with data on some future series of patients treated without tuberculin or with some other therapeutic agent.

2. *Syphilis*.—The criteria for a definite diagnosis of syphilitic uveitis were as follows: 1. A characteristic uveal lesion, with nodules or gummas, occurring either in early or in late syphilis but in the proper time relation to the acquisition of the syphilis. 2. A lesion which was noncharacteristic of syphilis but which occurred at the proper stage of early syphilis and responded favorably to antisyphilitic treatment. 3. A uveal lesion appearing noncharacteristic, occurring in late syphilis and responding favorably to proper antisyphilitic treatment in a patient with no other demonstrable etiologic factor. In the three groups of patients

the diagnosis of systemic syphilis was clearly established by positive serologic reactions and by physical examination.

The criteria for a presumptive diagnosis of a syphilitic origin of the uveitis were: 1. The presence of systemic syphilis and a favorable response of the ocular lesion to antisyphilitic treatment, even though other possible etiologic factors were found. 2. The presence of syphilis and the exclusion of other etiologic factors, even though the response to antisyphilitic therapy was unsatisfactory.

The characteristic syphilitic ocular lesions include the well known "salt and pepper" fundus of congenital syphilis, the iritis associated with interstitial keratitis in congenital syphilis, the iritis rosacea, nodosa and papulosa occasionally seen in association with the uveal lesions of early acquired syphilis and the gummatous lesions of late syphilis. The noncharacteristic lesions include the serous or plastic iritis of early acquired syphilis, the diffuse choroiditis of early syphilis and the generalized uveitis of late acquired syphilis.

Obviously, with the history, physical examination, serologic tests and response to antisyphilitic therapy pointing to syphilitic uveitis a positive diagnosis presents little difficulty. For this reason the greater number of syphilitic patients can be classified in group 1, as having clearcut diagnoses.

A serologic test for syphilis was performed on every patient in this series, but only 69 patients showed evidence of the disease (either serologic or clinical). The total number of patients with uveitis actually attributed to syphilis, both definite and probable, was 59, or 10.5 per cent of the entire series. Of these, 36 had syphilitic iritis, 7 had choroiditis and 16 had generalized uveitis. Twenty-two had congenital syphilis and 37 acquired syphilis.

The most interesting feature of the syphilitic group is the small number of patients with choroiditis. Of the total of 7 such patients, 4 had the ordinary choroiditis of congenital syphilis and only 3 the choroiditis due to acquired syphilis. In the pre-Wassermann days syphilis was regarded as the commonest cause of choroiditis and in many clinics mercurial inunctions were almost routine treatment for every patient with choroiditis. With the advent of the Wassermann reaction and the increasing knowledge of the symptomatology of syphilis, the choroiditis of fewer and fewer patients is being attributed to syphilis. The diffuse choroiditis of secondary syphilis is undoubtedly one of the most serious forms of ocular syphilis and the one which probably makes most urgent the hospitalization of the patient. It is therefore interesting that in a large general hospital with an active syphilis clinic, from which a continuous stream of syphilitic patients with ocular lesions are referred to the ophthalmic department, there were encountered in fourteen years only 3 patients with choroiditis from acquired syphilis of sufficient severity to warrant admission of the patient to a ward.

The low percentage in this series of patients with uveitis attributed to syphilis is probably due to the fact that in general only patients with obscure or severe uveitis were admitted to the hospital. Since the diagnosis of syphilitic uveitis as a rule presents little difficulty and since proper treatment can usually be carried out as well in the outpatient department as in the wards, patients with this diagnosis are not usually admitted to the hospital. A further factor is that with the earlier recognition of syphilis and with the availability of adequate treatment for the disease the incidence of syphilis in certain communities is doubtless decreasing, and this is reflected in a decreased incidence of syphilitic uveitis.

3. *Sarcoid and Brucellosis*.—This study is of no value with regard to the incidence of uveal disease due to either of these causes. The 3 patients classified as having sarcoid were encountered late in the series, when our attention had become focused on the ocular changes of this disease. Each had other obvious clinical manifestations of sarcoid. Doubtless an earlier recognition of the importance of sarcoid in ophthalmology would have led to the recognition of the condition in a few other patients, probably erroneously classified as having tuberculosis. The same can be said for brucellosis. Only 2 patients with this condition are included in this series, one a patient with actual bacteriologic evidence of undulant fever and the other a patient with serologic evidence of brucellosis and no other apparent etiologic factor. Both sarcoid and brucellosis are now considered in the study of every case of uveitis, and at a later date we hope to present a report which will give some information on the relative importance of these factors as causes of uveal disease.

4. *Foci of Infection*.—The criteria adopted for a definite diagnosis of an etiologic relationship between uveitis and foci of infection were: That there should be a demonstrable focus of infection in the teeth, tonsils or accessory nasal sinuses or a nongonorrheal infection of the genitourinary tract and in addition (1) that the uveitis have followed the onset or an exacerbation of activity in the focus of infection, (2) that the ocular inflammation show a definite alteration after eradication of the focus of infection (either an abrupt healing or a local intensification of the inflammation followed by healing) or (3) that the uveitis exhibit the acute serous type of reaction usually believed due to foci of infection, that there be a demonstrable focus of infection severe enough to produce definite symptoms of itself and that the complete diagnostic survey have revealed no other etiologic factor to which the uveitis might logically or probably be attributed.

The criteria for a probable diagnosis of an etiologic relationship between uveitis and foci of infection were that the ocular lesion show none of the characteristic changes produced by the infectious granulomas

and that the diagnostic survey should have revealed no other factor to which the uveitis might logically be attributed and have revealed a clinical focus of infection, even though it was asymptomatic.

The requirements for a definite diagnosis of a relationship between uveitis and foci of infection cannot be regarded as too rigid. They do not necessitate any supporting serologic or other laboratory evidence of undue systemic reactivity to organisms isolated from the focus of infection. For several years attempts were made to cultivate organisms from suspected foci of infection and determine the patient's reactivity to the isolated strains as evidenced by cutaneous reactions and certain laboratory procedures. These proved to be inconclusive diagnostic procedures, the patients and controls reacting indiscriminately to the various common pathogenic organisms isolated. This approach was therefore abandoned. Even with the somewhat mild requirements adopted, the uveitis in only

TABLE 14.—*Incidence of Dental and of Sinus Infections in 523 Patients with Endogenous Uveitis and in 507 Controls **

	Focus of Infection	
	Dental Infection	Sinus Infection
Patients with uveitis.....	27.1%	12.1%
Control patients.....	25.8%	13.0%

* The figures listed for the control patients are corrected statistically to conform with the age distribution (by decades) for the patients with uveitis. The incidence of these infections in patients with cataract (forming part of the control series) was obtained from a current study by Dr. W. F. Hughes on the results of cataract extractions.

5.5 per cent of the patients in this series could be "definitely" attributed to foci of infection.

The criteria for a probable diagnosis are even more elastic. To illustrate the extent to which they are open to criticism, the histories of a control series of patients without endogenous ocular disease were studied with regard to the incidence of foci of infection. A total of 507 patients with cataract, ocular trauma, etc., were found in whom a careful search had been made for foci of infection in the teeth and in the sinuses. The relative incidences of foci of infection in this control group and in 521 patients¹¹ with endogenous uveitis were found to be almost identical (table 14).

There is, therefore, an element of doubt as to the accuracy of any diagnosis in which uveitis is attributed to a focus of infection. In view of the widespread acceptance of the doctrine of focal infection and

11. Of the 562 patients in the whole series only 521 had complete surveys made for foci of infection. The diagnoses for the remaining 41 patients were made either on histologic evidence or on clinical findings which permitted a positive diagnosis irrespective of the presence of foci of infection.

the importance it has in the practice of clinical ophthalmology, it is worth while to review briefly the evidence for and against the general theory of focal infection.

The concept that primary foci of infection cause certain remote secondary inflammations was suggested during the latter part of the nineteenth century, but did not gain widespread popularity until the second decade of the twentieth century, when it was elaborated chiefly by Billings¹² from 1912 to 1916. This concept assumes that from a primary focus of infection, which is a circumscribed area of tissue harboring exogenous pathogenic organisms and usually located adjacent to a mucous or cutaneous surface, infecting organisms may spread by hematogenous pathways to remote tissues of the body and there produce secondary foci of infection. If primary diseased foci, such as the teeth, tonsils or organs of the genitourinary tract, which might obviously become infected from external sources, can produce a transient bacteremia and the bacteria thus introduced in the blood stream become lodged in the endocardium, joints or eyes, the causation of infections of these tissues is clear. Thus the theory of focal infection offered a logical solution for many of the problems of localized endogenous infections, and it easily gained widespread acceptance.

During the same period Rosenow¹³ published dramatic reports on the environmental transmutation of bacteria and on the experimental production of diseases of the joints, endocardium, gallbladder, stomach and other organs by the injection of bacteria isolated from similar infected organs in human beings. His consequent theory as to the elective affinity of various strains of bacteria for particular organs supported the concept of focal infection and afforded an explanation for the different types of localized secondary infection (e. g., arthritis and iritis) which might occur. As a result of the doctrine of focal infection there ensued a wholesale and often indiscriminate eradication of possible foci as a therapeutic procedure for a great number of pathologic conditions, and the literature soon became filled with reports of brilliant cures of various obscure diseases following the removal of teeth or tonsils, the drainage of nasal sinuses and similar procedures.

12. Billings, F.: *Focal Infection: The Lane Medical Lectures*, New York, D. Appleton and Company, 1916.

13. Rosenow, E. C.: *J. Infect. Dis.* **6**:245, 1909; **7**:411 and 429, 1910; **14**:1 and 61, 1914; **16**:240 and 367, 1915. Rosenow, E. C., and Sanford, A. H.: *ibid.* **16**:219, 1915. Rosenow, E. C.: *The Newer Bacteriology of Various Infections as Determined by Special Methods*, *J. A. M. A.* **63**:903 (Sept. 12) 1914; *Bacteriology of Cholecystitis and Its Production by Injections of Streptococci*, *ibid.* **63**:1835 (Nov. 21) 1914. Rosenow, E. C., and Osterdal, S.: *The Etiology and Experimental Production of Herpes Zoster*, *ibid.* **64**:1968 (June 15) 1915. Rosenow, E. C.: *J. Infect. Dis.* **17**:403, 1915.

However, it soon became apparent that in many instances the sacrifice of teeth or tonsils or any other procedure involved was without effect on the diseased condition for which it had been undertaken, and more critical observers began to question various aspects of the concept of focal infection. Most competent bacteriologists, while recognizing the different environmental requirements of different bacteria, were unable to confirm in any way the elective affinity of various strains of bacteria for specific tissues. It was pointed out that primary foci of infection were frequent in persons in whom secondary foci never developed and also that it was peculiar for secondary infections to result from rather small foci in the teeth or tonsils and not from such massive infections as empyema or psoas abscess. Laboratory investigations pertaining to the demonstration of any undue systemic reaction to organisms cultured from primary foci (such as the complement fixation test and determination of the agglutination titer and the cutaneous reactivity) were in the main futile, most normal and most diseased persons showing more or less reactivity to common pathogenic organisms to which they were constantly exposed.

Despite these various objections, in the decade following Billings' articles the doctrine of focal infection became firmly ingrained in American medical practice and the search for primary foci of infection and their eradication became a procedure generally accepted, especially by ophthalmologists, in the treatment of many endogenous infections. In 1928 Holman¹⁴ summarized the literature, including that on laboratory investigations, in a critical review. While accepting a causal relation in many instances between primary foci of infection and remote disease, he pointed out the impossibility of deciding with certainty if any determined focus was causally related to the secondary disease and the fruitlessness of efforts to develop procedures of any diagnostic accuracy in this regard.

Even with the conservative reservations of Holman, however, the case for the original concept of focal infection was far from settled. Critics of the theory freely conceded that the origin of systemic diseases such as gonorrheal arthritis, septicemia and tetanus lies in primary foci of infection, but the idea that various diseases of unknown origin are related to infections of the teeth, tonsils and other such localized foci met with steadily increasing opposition. In 1940 Reimann and Havens¹⁵ ably summarized these views, especially with regard to infection of the teeth and tonsils. These authors took the view that most "infected" teeth

14. Holman, W. L.: Focal Infection and "Elective Localization," *Arch. Path.* 5:68 (Jan.) 1928.

15. Reimann, H. A., and Havens, W. P.: Focal Infection and Systemic Disease: Critical Appraisal; Case Against Indiscriminate Removal of Teeth and Tonsils, *J. A. M. A.* 114:1 (Jan. 6) 1940.

or tonsils removed in the eradication of primary foci are no more infected than is physiologic and serve as entries for bacteria into the blood stream no more than other mucous surfaces within the body. The existing clinical evidence as exemplified by various comprehensive reports is actually against the idea that the removal of so-called infected teeth or tonsils is of clinical benefit in such diseases as rheumatic fever, rheumatoid arthritis, subacute bacterial endocarditis and nephritis. For example, statistical studies show that regardless of the type of treatment used for rheumatoid arthritis about 25 per cent of the patients "recover," 50 per cent improve and 25 per cent get worse. Bauer's¹⁶ observation that in a series of 300 arthritic patients those with their teeth let alone actually did better than those subjected to oral operations and Pemberton's¹⁷ similar observation with regard to removal of tonsils in a series of 400 arthritic patients certainly form strong evidence against the concept of focal infection as it was formerly taught and practiced.

The ophthalmologic literature, however, is replete with reports, too numerous to list, of the dramatic recovery of patients with uveitis following the removal of primary foci of infection in the teeth, tonsils, nasal sinuses or genitourinary tract. Most of the reports on the relationship of disease of the uveal tract to focal infection emphasize some special etiologic factor. The following examples are typical: Kapuszenski¹⁸ reported 51 cases of iridocyclitis caused by infections about the teeth, with healing after extraction of the diseased teeth. Vom Hofe¹⁹ reported 13 cases of endogenous ocular inflammation believed due to infected tonsils. Lagrange and Goulesque²⁰ stressed the importance of sinus infection. Benedict²¹ reported 14 cases of uveitis believed to be caused by infection in the female pelvis. Johansson²² expressed the belief that latent phlebitis might often be the cause of iridocyclitis. Davies²³ reported 3 cases of iritis which he believed was related to urinary infection. Dwyer²⁴ considered an abnormal intestinal flora the most important cause of uveitis.

The majority of reports such as those cited are open to the criticism that they emphasize some one factor believed to be of importance and do not give a complete view of the clinical picture and so do not allow

16. Bauer, W. W.: Personal communication to Reimann and Havens.¹⁵

17. Pemberton, R.: *Arthritis and Rheumatoid Conditions: Their Nature and Treatment*, ed. 2. Philadelphia, Lea & Febiger, 1935.

18. Kapuszenski, W.: *Ann. d'ocul.* **172**:817, 1935; abstracted, *Klin. Monatsbl. f. Augenh.* **95**:833, 1935.

19. vom Hofe: *Klin. Monatsbl. f. Augenh.* **101**:596, 1938.

20. Lagrange, H., and Goulesque, J.: *Ann. d'ocul.* **175**:493, 1938.

21. Benedict, W. L.: *Wisconsin M. J.* **32**:85, 1933.

22. Johansson, E.: *Ztschr. f. Augenh.* **92**:154, 1937.

23. Davies, L.: *Tr. Ophth. Soc. U. Kingdom* **37**:220, 1917.

24. Dwyer, J. G.: *Arch. Ophth.* **48**:344, 1919.

any deductions as to the relative importance of focal infection and of other etiologic factors in the production of the uveal disease. The observation of Enroth²⁵ that a great many cases of iritis occurred when there was a sharp climatic change is of greater significance, suggesting that the well known intensification of infection in primary foci and the changes in capillary permeability after exposure to cold predispose to the outbreak of secondary foci. The report of Zanettin,²⁶ who found only an 18 per cent incidence of tonsillar infection in 87 patients with noninfectious ocular disorders, such as glaucoma or cataract, as compared with a 57 per cent incidence in 26 patients with inflammatory ocular diseases, would be of significance except that it lacks any sort of confirmation.

The most significant clinical evidence in the literature with regard to the importance of foci of infection in the causation of uveitis is contained in the report of Irons and Brown²⁷ published in 1926. These authors were able to conduct a follow-up study of 50 of the 200 patients with iritis whom they had examined and classified three to twelve years previously (table 1). Of these 50 patients 46 per cent had had previous attacks of iritis. Of the 40 patients with iritis originally believed due to foci of infection, the primary focus had been effectually removed in 33 and not one of these suffered a recurrence of iritis. Two of the 7 patients in whom the primary foci had not been eradicated had recurrences of iritis. A sinus infection which persisted in spite of treatment was blamed in one of these, while infected tonsils which were not removed were blamed in the other.

There is a moderate amount of experimental work dealing with the relationship of ocular disease and focal infection. When animals are given intravenous injections of living bacteria, metastatic lesions occasionally, sometimes frequently, occur in the eye.²⁸ These lesions usually present the picture of endophthalmitis and only occasionally simulate the clinical lesions of the uveal tract attributed to focal infection. Further, while lesions do occur in the eye, they likewise occur in diverse organs such as the liver, spleen and kidneys, and there is vastly more experimental evidence against oculotropism and the elective affinity of bacteria than there is for these suppositions. Berens and his co-workers²⁹ have described studies indicating that a high agglutination titer to an autoge-

25. Enroth, E.: *Acta ophth.* **10**:146, 1932.

26. Zanettin, G.: *Ann. di ottal. e clin. ocul.* **62**:588, 695 and 786, 1934.

27. Irons, E. E., and Brown, E. V. L.: *Recurrence of Iritis as Influenced by the Removal of Infections*, *J. A. M. A.* **87**:1167 (Oct. 9) 1926.

28. Chojnacki, P.: *Arch. f. Ophth.* **139**:288, 1938. Zanettin.²⁶

29. Berens, C.; Connolly, P. T., and Chapman, G. H.: *Brit. J. Ophth.* **18**: 463, 1934. Berens, C.; Nilson, E. L., and Chapman, G. H.: *Am. J. Ophth.* **19**: 1060, 1936. Berens, C.; Angevine, D. M.; Loren, G., and Rothbard, S.: *ibid.* **21**: 1315, 1938.

nous strain of streptococci is strong presumptive evidence that the strain is related to coincident ocular disease, although the converse is not true. They stated the belief that the use of a number of different serobacteriologic reactions and animal toxicity tests often forms a reasonable basis for an evaluation of any autogenous organism as a focal invader. While this line of investigation is highly reasonable, most such studies, including those dealing with undue cutaneous sensitivity to bacteria isolated from a primary focus of infection, are hopelessly complicated by the fact that the majority of normal persons react to some unpredictable extent against the common organisms usually encountered in foci of infection. Bacteremia has occasionally been reported during the acute stages of uveitis,³⁰ but so infrequently as to have no significance.

A critical review of the evidence for and against the original theory of focal infection yields little doubt that this theory at present rests on shaky grounds. The causal relationship of foci of infection to uveitis is no better substantiated than the causal relationship of such foci to infectious arthritis or rheumatic fever. The figures presented in this statistical study do little to support the idea of a frequent relationship of uveitis and primary foci of infection. In contrast to the studies of Irons and Brown, who attributed the uveitis in 63 per cent of their cases to focal infection, in this series the uveitis could be attributed to such foci with fair certainty in only 5.5 per cent and by a stretch of the imagination in only an additional 20.6 per cent.

Likewise, the figures relative to the effect of removal of foci of infection on the recurrence of uveitis in the patients in this series who could be adequately followed are in sharp contrast to the figures reported by Irons and Brown. Table 15 gives these figures for 74 persons in whom the uveitis was believed probably due to foci of infection and who were followed over an average period of four and three-tenths years. In 21 of these patients the various foci of infection had not been eradicated, in 11 the foci had been partially cleared up and in 42 as far as could be ascertained clinically all foci of infection had been removed. The incidence of recurrence was 29 per cent in patients in whom the foci of infection were utterly neglected, 36 per cent in patients in whom the foci had been partially removed and 33 per cent in patients in whom all foci had been removed.

While it is indisputable that many cases of endogenous uveitis are encountered in which there is no demonstrable cause other than foci of infection and while there is occasionally suggestive evidence of a cause and effect relationship, it is likewise true that exactly similar cases occur without evidence of other etiologic factors and without any demonstrable focus of infection. How may this enigma be explained?

30. Traut, E. F.: *Am. J. Ophth.* **17**:106, 1934.

A newer and broader concept presupposes that all mucous membrane and cutaneous surfaces, as well as definite localized infections, may act as potential portals of entry for bacteria into the blood stream. That bacteria do constantly enter the blood stream in small numbers in normal persons is well known. For example, colon bacilli can often be cultivated from the portal vein; pyelitis develops with amazing regularity if there is an obstruction to the ureter, and the source of infection can be conclusively traced to intermittent bacteremia, the kidney being infected only because predisposed by the local condition.

Assuming that bacteria do constantly gain access to the blood stream, a ready explanation for the selective occurrence of various endogenous inflammations is afforded by the concept of localized hypersensitivity of tissue. It is well known that there occurs such hypersensitivity to various substances, including bacterial antigens. If bacteria, not necessarily pathogenic, occasionally reach the uveal tract they may well create there a localized sensitivity. Any subsequent bombardment of this

TABLE 15.—*Effect of Removal of Foci of Infection on Recurrences of Uveitis*

Treatment of Foci of Infection	No. of Patients	Average Period Followed, Years	Previous Attacks	Recurrences
Not removed.....	21	4.2	67%	29%
Partially removed.....	11	3.8	73%	36%
Totally removed.....	42	1.5	55%	33%

sensitized focus by these antigens absorbed from cutaneous or mucous membrane surfaces and carried in the blood stream would cause a local inflammation. In fact, such inflammation can readily be produced in experimental animals.³¹ A mechanism of this sort not only would explain the endogenous uveitis but would likewise explain the impossibility of culturing bacteria in material from the affected eye. The clinical proof of this hypothesis, however, is lacking because of the absence of any means of demonstrating local hypersensitivity of the uveal tract in patients; nor is it likely to be forthcoming, on account of obvious technical difficulties.

In summary, it may be fairly stated that the role of foci of infection in the causation of endogenous uveitis is far from settled. Despite the negative evidence presented in this report, primary foci of infection may in some instances undoubtedly be the direct cause of the uveitis. But their role in the production of endogenous ocular disease is certainly not as great as once believed, and little or nothing is to be gained by the indiscriminate eradication of infections of the teeth, tonsils, sinuses and genitourinary tract. A reasonable method of handling such infec-

31. MacLean, A. L.: Tr. Am. Ophth. Soc. **34**:324, 1936.

tions in patients with uveitis would be to treat them in exactly the same manner as though no uveitis were present—radical procedures being employed only when the infection was sufficiently severe to warrant them in any event.

5. *Gonococcic Infections*.—The criteria for a positive diagnosis of gonococcic uveitis were that the clinical appearance and course of the ocular lesion should be compatible with a gonococcic infection, that the first attack have occurred during the course of active gonorrheal urethritis or prostatitis or in conjunction with gonococcic arthritis and that the diagnostic survey have disclosed no other etiologic factor to which the ocular lesion might be more logically attributed.

The criteria for a presumptive or probable diagnosis of gonococcic uveitis were that even though there was no active gonorrhea or arthritis at the time of the first ocular inflammation the diagnostic survey should have disclosed no other etiologic factor to which the uveitis might logically be attributed and that there be a history of gonorrhea or a positive reaction to the complement fixation test for gonococci.

In establishing the existence of healed gonococcic genital infection, a negative history is often unreliable. Unfortunately the complement fixation test for gonococci occasionally gives a false positive reaction, usually because of a close antigenic relationship to *Brucella*, but when a sensitive gonococcus antigen is used the test almost always gives a positive reaction if the patient has ever had gonorrhea. Thus the complement fixation test is of principal value in ruling out the possibility of gonorrhea as a cause of uveitis.

It is evident that the criteria for a positive diagnosis, though as rigid as possible, may leave some doubt of the gonococcic origin of the ocular disease. The criteria for a probable diagnosis are even more open to criticism and leave much uncertainty as to the accuracy of the diagnosis. In a discussion of the etiologic diagnosis it is therefore worth while to inquire into just what the usual appearance and course of gonococcic iritis may be and just what is the pathogenesis of the ocular lesion.

During the nineteenth century the only ocular inflammations attributed to gonococcic infection were the iridic inflammations occurring for the first time during the course of active genitourinary gonorrhea or gonococcic arthritis. During the first part of that century only anterior uveitis of an acute, fibrinous type was classified as gonococcic. It soon became apparent, however, that in only a part of the cases of ocular disease related to gonococcic infection was there a violent inflammation characterized by exudation of fibrin into the aqueous. Of the 112 case reports reviewed by Byers³² in 1908, gelatinous anterior chamber

32. Byers, W. G.: *Gonorrheal Ocular Metastases*, in *Studies from the Royal Victoria Hospital, Montreal*, 1908, vol. 2, no. 2.

exudates were described in only 13 and hemorrhagic exudation in 3, various degrees of nonspecific inflammation being described in the remainder. It is therefore apparent that no definitely characteristic appearance can be ascribed to gonorrheal iritis. While at first the ocular disease was considered gonococcic in origin only in cases in which the anterior part of the uvea was involved, Byers found reports of 9 cases in which there was also associated choroiditis, and it is possible therefore that choroiditis due to gonococcic infection may occur with or without associated iritis. Griffith (1900)³³ increased the realm of possible gonorrheal uveitis by suggesting that iritis not only can be a complication of an active gonorrheal infection but may be a late and the only sequel.

A diagnosis of gonococcic uveitis can therefore never be made with certainty from the clinical picture alone. Acute, violent anterior uveitis characterized by exudation of fibrin and occasionally blood into the anterior chamber, by the absence of discrete keratic precipitates and by a tendency to rapid healing with slight residual damage but frequent recurrences is generally regarded as the "characteristic" ocular picture. However, a number of patients observed in the Wilmer Institute with exactly this type of uveitis gave a history negative for gonorrhea and showed neither clinical nor laboratory evidence of active or healed gonorrhea. In the present series 4 of the patients with definite and 6 with probable gonococcic uveitis exhibited the so-called characteristic anterior chamber exudates, while 35 of those classified in other etiologic groups had the same type of inflammatory response. A larger number of patients with either definite or probable gonococcic iritis had a milder form of acute iritis which rapidly subsided with almost no residual change or a plastic type of acute uveitis which sometimes became chronic and often caused extensive posterior synechias or complicated cataract. All showed a marked tendency to recurrence, and some had as many as fifteen or twenty relapses over a period of years.

The possible pathogenesis of ocular lesions due to gonococcic infection is most interesting. Although the gonococcus was not discovered until 1879, the occasional occurrence of iritis in patients with gonorrheal urethritis and more particularly in those in whom concomitant arthritis developed was clearly recognized as early as 1830 (Cooper³⁴), and Mackenzie³⁵ in his classic text (1833) gave a full description of typical gonorrheal iritis which even today can hardly be improved on. The relationship between gonorrhea, arthritis and iritis has been observed with such frequency as to preclude any doubt as to the actual causation of

33. Griffith, J.: *Tr. Ophth. Soc. U. Kingdom* **20**:83, 1900.

34. Cooper, cited by Byers.³²

35. Mackenzie, W.: *A Practical Treatise on Diseases of the Eye*, Boston, Carter, Hendee & Co., 1833.

uveal inflammation by the gonococcus. Whether the inflammation is a result of actual metastatic infection or is an allergic type of reaction analogous to that assumed in cases of "focus of infection" is not certain. Sidler-Hugenin³⁶ was able to culture gonococci in material from the anterior chamber of 1 of 4 patients with acute gonorrheal iritis, but this patient also had a positive blood culture and a hemorrhage in the anterior chamber; other investigators (Byers³² and Browning³⁷) have been unable to recover the organism from the eye. In favor of there being an actual metastatic infection is the fact that gonorrheal arthritis, generally regarded as being a definite metastatic infection of the synovia, is frequently associated with the uveitis. However, it should be pointed out that gonorrheal arthritis can be divided into two types, one type being characterized by a purulent exudate which contains no demonstrable antibodies and from which gonococci can be cultured and the other characterized by a less cellular exudate which has a high antigonococcus titer and from which gonococci cannot be cultured (Keefer and Spink³⁸). Which type is usually associated with iritis has not been determined. Suggestive of an allergic type of reaction is the fact that typical gonorrheal iritis is never observed until two to six weeks after the onset of a first attack of gonorrheal urethritis, always occurring after the infection has persisted for some time in the posterior portion of the urethra or in the prostate.

Relapses of the ocular inflammation can and frequently do occur without relation to recurrences of the urethritis, prostatitis or arthritis. The frequent recurrence of uveitis long after the primary gonococcic infection has been clinically eradicated is confusing. It is supposed by many investigators that clinically undetectable gonococci may lie dormant in the prostate or in other organs for many years and occasionally enter the blood stream in small numbers. If this view is correct it is logical to believe that a primary attack of uveitis may sometimes occur as a late and the only manifestation of clinically "healed" genitourinary gonorrhea, but this must remain a matter of conjecture. It is also possible that an original attack of gonococcic uveitis alters the local immune and sensitivity reactions and predisposes the eye to inflammation by other transient bacteremias. This view is supported by the fact that chemotherapy with sulfanilamide compounds, which should usually eradicate gonococci from the body, is totally without effect in preventing late relapses of iritis.^{9c}

6. *Nongranulomatous Systemic Infections*.—The associated condition of the 33 patients whose uveitis was attributed to a general systemic

36. Sidler-Hugenin: Arch. f. Augenh. 69:346, 1911.

37. Browning, S. H.: Brit. J. Ophth. 4:102, 1920.

38. Keefer, C. S., and Spink, W. W.: Gonococcic Arthritis: Pathogenesis, Mechanism of Recovery and Treatment, J. A. M. A. 109:1448 (Oct. 30) 1937.

infection other than an infectious granuloma is shown in table 16. A total of 14 patients were encountered in whom there was no other apparent cause for the uveitis and its occurrence in close association with systemic infection indicated a definite cause and effect relationship. In the other 19 patients also there was no other apparent cause for the uveitis but the ocular inflammation was not definitely associated with a general systemic infection and permitted little more than a presumptive diagnosis of a cause and effect relationship. In the 33 patients in these two subgroups the uveitis was in no way characteristic and the absence of all nodular lesions was noteworthy.

Seven of the 14 patients classified as having uveitis definitely related to systemic infection had infectious arthritis. In several of them definite foci of infection were present, and obviously it may be argued that both the iritis and the arthritis were the result of bacterial metastasis from these primary foci. However, in the light of existing knowledge of arthritis it is more probable that both were manifestations of bacterial hypersensitivity—the source of the intoxicating allergins being either

TABLE 16.—*Uveitis Associated with Nongranulomatous Systemic Infections*

Relationship Between Conditions	No. of Patients	Infectious Arthritis	Rheu- matic Fever	Influenza	Meningo- coccal Septi- cemia	Strepto- coccal Septi- cemia	Peri- arteritis Nodosa	Unknown Systemic Infection
Definite.....	14	7	0	4	2	1	0	0
Indefinite.....	19	1	3	0	0	0	1	14

the manifest foci of infection or some clinically uninfected mucous membrane surface. Intravenous administration of streptococcus vaccine according to the method recommended by Wainwright³⁹ in the treatment of arthritis was attended by healing in 2 of these patients, with a recurrence of uveitis several months after cessation of vaccine therapy in 1. In view of the great stress laid on the association of arthritis and iritis in the last century it is noteworthy that this association was found in only 8 patients, or 1.4 per cent of the entire series. Three patients had uveitis and acute rheumatic fever at the same time, and no other plausible explanation for the iritis was found. The cause and effect relationship in these cases is classed as probable.

The histories of the 3 patients in whom the uveitis occurred in conjunction with either meningococcal or streptococcal septicemia are in no way remarkable. The uveitis was not metastatic endophthalmitis (patients with which are not included in this series) but was ordinary iritis, and it is a justifiable hypothesis that it was the result of direct

39. Wainwright, C. W.: Gonococcal Arthritis: Pathogenesis, Mechanism of Recovery and Treatment, *J. A. M. A.* **103**:1357 (Nov. 3) 1934; *Ann. Int. Med.* **9**:245, 1935.

bacterial metastasis, with a small number of organisms, probably of low virulence, the normal bactericidal activity of the ocular fluid being sufficient to overcome the infecting organisms.

The histories of patients with uveitis occurring in association with influenza were interesting in that they may represent examples of actual virus disease in the eye. In 2 patients there was definite association of recurrent iritis with recurrent influenza. In 2 the association was not so definite but no other cause for the uveitis was apparent.

There were 14 patients whose uveitis was attributed to an unknown systemic infection. They were all apparently healthy persons in whom sharp active attacks of iritis developed. No etiologic factors were found to which the uveitis could be attributed. It was therefore assumed that some unknown systemic infection was responsible. The uveitis of these patients might equally well be classified as of unknown cause.

7. *Metabolic Disease*.—The etiologic diagnoses of 3 patients are grouped under this heading, the uveitis, however, probably being only coincident with and not caused by the metabolic disease. The metabolic disturbances were gout, diabetes and parathyroid tetany, respectively. The ocular and the general picture of these patients was in no way remarkable. It is notable that only 8 patients in the entire series showed any evidence of diabetes, in spite of the fact that a fasting determination of the blood sugar was routine. Also, fasting determinations of the blood uric acid in approximately half of the cases established a diagnosis of gout in only 1 instance.

8. *Miscellaneous*.—The histories of the 10 patients whose etiologic diagnoses are grouped under this heading are in no way remarkable, except that of a patient with iritis due to iodism which has been individually reported (Goldberg⁴⁰). In 2 patients uveitis occurred as a complication of herpes zoster and in 3 as a complication of herpes simplex. Two patients had the poliosis-vitiligo syndrome. The uveitis was associated with a probable virus meningitis in 1 and with Raynaud's disease in 1. In these patients there was nothing characteristic in the ocular picture.

SUMMARY

A series of 562 case histories of endogenous uveitis is analyzed. The patients were admitted to the wards of the Wilmer Ophthalmological Institute of the Johns Hopkins Hospital between Nov. 1, 1925 and July 1, 1939. No outpatients are included. These patients therefore comprise a group with uveitis more severe than the average. A total of 327 patients were followed for more than one year.

Each patient was subjected to a diagnostic survey, which became gradually more extensive as the importance of additional factors in the

40. Goldberg, H. K.: *Am. J. Ophth.* 22:65. 1939.

causation of uveitis were more fully realized. In general the diagnostic survey consisted of the taking of a complete medical history; a general physical examination; special examinations of the nose, throat, nasal sinuses, teeth and urogenital systems; serologic tests for syphilis, and the intracutaneous determination of sensitivity to tuberculin. Roentgenograms of the chest were made in 287 instances, and the complement fixation reaction for gonococci was determined for almost all patients examined after 1936. Special bacteriologic studies of foci of infection were made in some instances, and various sensitivity tests were carried out when indicated. Serologic tests for brucellosis and biopsy of a lymph gland for sarcoid in patients with nodular iritis were not made routine until the conclusion of this study.

In the etiologic classification, the series was divided into two groups. In group 1 are included those 244 patients in whom the evidence was sufficiently clear to justify a relatively definite conclusion as to the cause of the uveitis. In group 2 are included the remaining 314 patients. In these the evidence was considered either too scanty or too conflicting to permit more than a fair guess as to the cause of the uveitis. The results in group 1, group 2 and in a series as a whole are shown in table 6.

The criteria for etiologic classification are discussed and the cases in each etiologic group analyzed. The following points are emphasized:

1. That uveitis may often, if not usually, be recognized clinically as granulomatous or nongranulomatous.

2. That a diagnosis of ocular tuberculosis must depend more on the clinical picture and the exclusion of other factors than on tuberculin reactions and roentgenograms of the chest or response to tuberculin therapy.

3. That syphilitic uveitis is usually easy to diagnose and that acquired syphilitic choroiditis is very rare.

4. That in this group of patients foci of infection were no more common than in a control group and that removal of infected foci did not reduce the incidence of recurrence of uveitis.

5. That in most cases nongranulomatous uveitis can be explained on the basis of a local ocular sensitivity developing from a transient bacteremia. Such a transient bacteremia may arise from a clinically non-infected mucous surface as well as from a clinically infected surface.

ABSTRACT OF DISCUSSION

DR. WALTER F. DUGGAN, Utica, N. Y.: The uveitis in only 2.3 per cent of the authors' cases was not related to an infection. Their approach to the problem has been based on the premise of an infectious origin. Are their criteria for the positive diagnosis of tuberculous uveitis universally accepted?

Kemp stated that the absolute diagnosis of ocular tuberculosis is established only when bacilli are found on section. Tubercles occur in sympathetic ophthalmia. If these are not due to tuberculosis are the tubercles of other types of uveitis due to tuberculosis?

Nodules are said to be of diagnostic importance. Davids has stated that nodules or granulomas in the eye can be due either to specific or to nonspecific causes. Marchesani interpreted nodules and granulomas as allergic hyperergic inflammations.

An enormous body of observations showing the relation of environmental changes to physiologic and pathologic processes has been compiled by W. F. Petersen in "The Patient and the Weather." Petersen summarized 35 attacks of uveitis in which the onset could be correlated with sudden changes in the weather and said, ". . . even an iritis may be . . . responsive to changes in the meteorological environment." He expressed the belief that the meteorologic factor is a conditioning factor in the constellation of events influencing both physiologic and pathologic processes.

Many lesions attributed to focal infection or to tuberculosis represent a failure of homeostasis. The reactions causing the lesions are physiologic in nature but pathologic in degree.

An approach to the etiology of uveitis can be initiated from any point. On circumstantial evidence, histamine or histamine-like bodies can explain the uveities in many cases.

In man injections of histamine intensify positive reactions to intradermal tuberculin tests. Histamine is formed in the skin by the action of cold water or cold air and by cooling. This fact could explain the preponderance of acute uveitis in the cold months of the year and after chilling at any time. In herpes zoster ophthalmicus the antidromic impulses which act by liberating either histamine or H substance are the cause of the vesicles and could be the cause of the uveitis. This is a physiologic approach to the etiology of uveitis. It can explain the uveitis attributed to focal infection, infectious diseases, allergy, sympathetic ophthalmia, herpes and many other conditions. It does not explain the uveitis in every case because other substances occurring in the body can increase capillary permeability beyond physiologic limits.

In my opinion the uveitis in less than 2 per cent of cases is due to direct invasion of the uvea by bacteria. In many cases it is a manifestation of allergy or of hypersensitivity due either to bacterial allergens or to any substance which by its presence or absence can cause increased capillary permeability. Heat, cold, trauma, sudden variations in the meteorologic environment, drugs, serums, vaccines and sometimes the removal of foci of infection must be included among the exogenous factors which contribute to the development of uveitis. Endogenous factors include race, age, sex, constitution, heredity, disturbances in the local blood supply, subclinical avitaminosis, glandular dysfunction, variations in the concentration of various hormones in the blood, transient episodes of alkalosis and acidosis, autonomic imbalance, foci of infection and infectious diseases. All these factors can prepare the "soil" in which uveitis develops. A sudden change in one of them may precipitate the attack.

While the essayists have stressed the infectious or bacterial origin of uveitis, much evidence, both direct and circumstantial, would suggest

that in many cases the uveitis is not of bacterial origin and that even changes in the weather may be of etiologic significance.

DR. JOHN S. MCGAVIC, New York: The essayists have given an excellent statistical study on a large number of cases carefully studied under ideal clinical conditions. Such a report provides a standard for comparison for methods of determining the etiologic agent in patients with uveitis.

The authors believe that micro-organisms invade the uveal tract to produce uveitis. There is a great deal of evidence that uveitis can occur without the presence of organisms—even in the three diseases known to cause definite lesions in the uveal tract—syphilis, tuberculosis and gonorrhea. It is almost inconceivable that bacteria would not have been isolated more frequently than they have been if they were always present. Furthermore, a larger number of people with various systemic diseases would be expected to have uveitis during the course of these diseases.

The failure of sulfanilamide and its derivatives to affect uveitis, particularly the gonorrheal type, speaks against the absolute infectious origin of uveitis.

I am glad to hear an expression of doubt as to the value of the tuberculin test, and, although it may have significance in a large series of cases, such as that presented, I believe that in individual cases it has no practical value. Furthermore, it may be dangerous either in producing focal reactions or in precipitating secondary foci in the eye.

The authors have said that a focal reaction occurred in their patients and that this reaction was used to substantiate the diagnosis. Their wide experience in interpreting clinical findings seems to me to make the tuberculin test even less necessary in their cases than in the cases of the average ophthalmologist. In the therapeutic use of tuberculin they have observed focal reactions in 29 per cent of their cases. May this not mean a spread of the lesion, which, although it heals, will leave a large area of scarring? This is an important consideration in cases of lesions of the choroid lying near the macula.

If tuberculin is to be used at all, I believe that it should be used in minute doses. For hypersensitive persons there is doubt that the dose can be reduced sufficiently to avoid the occurrence of a focal reaction. I hope that the essayists will follow this study with study of a group of controls not treated with tuberculin.

After completing study of a given patient, one usually finds that one has not proved the uveitis to be due to brucellosis, lymphogranuloma venereum, tuberculosis or any focal infection but has a patient who has uveitis and may also have some systemic disease. The great difficulty comes in relating the disease to the uveitis, and indeed I believe that one seldom establishes an absolute diagnosis. This is obviously an unsatisfactory situation, and it is only by such painstaking statistical studies as the one presented by Dr. Guyton and Dr. Woods that ophthalmologists are brought up to date on this difficult problem and are stimulated toward more promising and more fruitful avenues of approach to it.

DR. T. L. TERRY, Boston: The figures in this study appear to represent the first even remote parallelism between American and European statistics on the causation of uveitis. It is my understanding from

European ophthalmologists that they do not accept so-called foci of infection as a common cause of uveitis, since almost invariably their clinic patients show infections of tonsils and around teeth, conditions which cannot be eradicated in the clinic services available.

Boeck's sarcoid as a cause of uveitis perhaps may appear to increase in frequency. I have seen uveitis associated with definitely proved sarcoid in at least 2 instances. Similarly, with the increased interest in infection due to *Brucella abortus*, this condition may be reported as an etiologic factor in uveitis with increasing frequency.

There is one point I wish to stress, namely the frequency of uveitis in association with malignant melanoma of the uvea. Uveitis is common with the choroidal neoplasm and with it is unilateral uveitis. Careful transillumination of the eye in 2 recent cases of unilateral uveitis led to my discovery of a tumor and removal of the eye. Therefore, in instances of unilateral uveitis, especially when one is unable to see the interior of the globe, a transillumination is in order.

DR. ALAN C. WOODS, Baltimore: Dr. Duggan brought up the question of finding bacilli in stained sections. If this is taken as the sole criterion for the diagnosis of tuberculous uveitis on histologic examination, a very small number of such diagnoses will be made. In the past seven years I have examined many rabbits' eyes with tuberculous uveitis produced by the intraocular injection of living bacilli. Only in a relatively small number could stainable bacilli be found. Every pathologist realizes the great difficulty of finding bacilli in sections of an eye with known tuberculous uveitis.

The second point brought forward by Dr. Duggan was his understanding that we considered tubercles in the iris a definite sign of tuberculosis. That is incorrect. We emphasized repeatedly in our paper that the presence of tubercles does not always mean tuberculosis. Such nodules are seen in sarcoid, in syphilis, in brucellosis and, in fact, in any of the infectious granulomas. They are a definite sign of an infectious granuloma, which may or may not be tuberculosis. To illustrate how closely nontuberculous nodules simulate true tuberculous nodules, the following experience is interesting. One day when I was examining a large number of tuberculous rabbits my associate, Dr. Burky, slipped 18 rabbits with brucellosis in with the group of tuberculous animals. I examined the entire group and did not recognize the difference between the clinical picture of experimental tuberculosis and that of brucellosis. Certainly the occurrence of nodules or tubercles on the iris is not an indication of tuberculosis but is an indication of what may be classed as infectious granuloma.

The third point concerned climatic changes and focal infection. The theory of their relation goes back many, many years. At the very genesis of the idea of focal infection Billings and Rosenow emphasized again and again that climatic changes might produce increased capillary permeability and might be one of the factors predisposing to the outbreak of uveitis from a focus of infection. I am far from denying that climatic changes may precipitate the onset of uveitis, but I do not believe for a moment that any climatic change *per se* can cause cellular infiltration with leukocytes, lymphocytes and epithelioid cells in the tissues of the eye. Climatic changes may have a great deal to do with the precipitation of an impending ocular reaction.

We have emphasized what we consider the importance of allergy and the sterility of the aqueous in practically all our cases in which it was tested. The idea of the sterility of the aqueous is not original, but goes back to the early work of Kolmer and numerous other investigators who tried endlessly to cultivate organisms from eyes with uveitis. This can only rarely be done. There is a great deal of evidence that many uveal lesions may be allergic in origin, but that they are is most difficult to prove clinically. Even in a patient with uveitis believed to be allergic and related to hypersensitivity to a specific organism isolated from a focus of infection, the actual relationship is almost impossible to prove. The patient may have a hypersensitive reaction to a cutaneous test with the suspected organism and a positive reaction to the agglutination test, and for the moment it may appear that the relationship is proved. However, if one then does the same tests on 10 patients with cataract in the same wards, 7 or 8 will give similar strong reactions. In other words, persons are exposed all their lives to the common organisms and frequently acquire a definite serologic reactivity to them. However, I do agree that uveitis in a great many cases is allergic in origin.

Dr. McGavic mentioned the relationship of micro-organisms to allergy. I can scarcely believe that uveitis is often due to actual bacterial metastasis of the organisms to the eye, except in syphilis. In my work in experimental ocular syphilis with Dr. Chesney we have been unable to demonstrate any specific hypersensitivity to the products of *Spirochaeta pallida*, although I admit we lack a satisfactory antigen. We do consistently find spirochetes in the eye. I am well aware of the theory that the interstitial keratitis of congenital syphilis is an allergic keratitis, but I do not agree with this viewpoint.

The question of the tuberculin test came up. Dr. McGavic has, I think, misinterpreted our paper on this. We have had no focal reactions in our diagnostic use of tuberculin. I think the intracutaneous Mantoux test is almost entirely free from the danger of producing a focal reaction in the eye. In 18 of our patients focal reactions did occur during the course of therapy. I have emphasized repeatedly that in tuberculin therapy the one essential is to keep the dose of tuberculin below the patient's point of reactivity—that there is no such thing as an absolute dose of tuberculin. Almost all of the focal reactions observed in the patients reported on in this paper occurred in patients who were taking tuberculin without proper supervision. Focal reactions are sometimes extremely dangerous. As a rule they are not. If the lesion lies close to the macula tuberculin must be used with the greatest of caution. That, however, is beside the present point.

Dr. Terry emphasized the importance of brucellosis and of sarcoid. I am in thorough agreement with him on that. Our figures are entirely worthless, as we have said, in regard to the incidence of brucellosis and of sarcoid.

In every case of uveitis since 1939 we have used all the routine serologic tests for brucellosis. Dr. Guyton and I both hope that when sufficient material has been accumulated, in the next three to four years, we can present a report which will give an idea of the importance of sarcoid and of brucellosis as a cause of uveitis. Sarcoid is apparently much more common than we formerly suspected, and undoubtedly the

uveitis in a few of our cases in which it was attributed to tuberculosis may have been due to sarcoid. Personally, I think it is histologically impossible to tell a sarcoid from a hard tubercle. There are a few refractile bodies in the nucleus of the giant cells.

It has been brought out that if the filtrate from a sarcoid is injected intracutaneously in a patient with sarcoid, a sarcoid nodule may be produced at the site of inoculation. In fact, it has been found that almost any inert substance, such as killed staphylococci, will produce a similar reaction. This peculiar reaction is of some value in the diagnosis of sarcoid. The biopsy of an excised gland is, however, of greater value. This, in connection with roentgenologic study of the bones and the mediastinum and search for the cutaneous lesions of sarcoid, is being undertaken now in all cases in which sarcoid is suspected, and more cases of sarcoid as well as a few cases of brucellosis have been recognized in the last two years. But these studies were undertaken so late that the inclusion of such cases would give an entirely false idea of the incidence of brucellosis and of sarcoid. We have emphasized our realization of the fact that many of our cases of brucellosis and of sarcoid may be erroneously classified as cases of tuberculosis.

I am in thorough agreement with Dr. Terry on melanomas.

AN UNUSUAL CASE OF HODGKIN'S DISEASE

A PRELIMINARY REPORT

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AND

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The usual general glandular involvement throughout the body in Hodgkin's disease is too well known to deserve more than passing comment. In comprehensive lists of organs and structures invaded mention is made of the eyeball, but a search of the literature has not revealed a report of cases of invasion of that structure.

Dr. W. G. MacCallum,¹ of the Department of Pathology of the Johns Hopkins University School of Medicine, gave the following information:

Sections from the eye in cases of Hodgkin's disease show some accumulation of cells in the choroid not characteristic, I think, of Hodgkin's disease but not found elsewhere. Our autopsies show no involvement of the eyes recognizable as part of Hodgkin's disease. It is possible that if the idea that Hodgkin's disease is due to *Brucella* infection is correct, examples of this infection involving the eye may be found, but such examples have not been found so far.

Dr. Andrew A. Eggston,¹ of the department of pathology of the Manhattan Eye, Ear and Throat Hospital, New York, stated:

I have never seen Hodgkin's disease involving the lymphatics of the bulbar conjunctiva. As a matter of fact, I do not recall having seen lymphatic involvement in any part of the orbit.

Hence the following case may be of interest.

Mrs. M. W., aged 50, American, a widow, a dress machine operator, was seen by one of us (J. W. A.) in April 1940. She complained of poor vision, especially in the left eye, which became painful after several hours of work; she mentioned an increasing growth on each globe, particularly the left, which interfered with closure of the lids, and she said that she had a "lump" in the left cheek and one in front of each ear. She thought that the mass in the cheek was increasing in size. Her history was interesting and perhaps significant. When she was about 7 years of age a "swelling" appeared under the chin and disappeared spontaneously after some days. At the ages of 8 and 9 it returned and ran the same course. These attacks were all in the winter. At 21 she had what was diagnosed as a goiter, into which medicine was injected several times. After some months, though apparently treatment had not been carried on continuously, the mass disappeared.

1. Personal communication to Dr. Avery.

In 1935 a painless lump was felt in the left cheek, and soon a reddish growth was seen on the left eyeball. Later one appeared on the right globe. These were not tender. Medical treatment was used without success. About one year after the invasions were first noticed by the patient the growths on the globes were excised. For six months the eyes were better. Then the growths appeared again in the same locations on the globes; the mass in the left cheek slowly increased in size, and lumps were felt in front of the ears, on both sides of the neck, at the elbows and in the groins. The patient was continuing at her work though she was weak and was losing weight, the vision was poor and the eyes were painful at the time of



Fig. 1.—*A*, the left eyeball, and *B*, the right eyeball on May 25, 1940.

the first examination by J. W. A., in April 1940. She also mentioned nasal blocking, which occasionally was complete and which seemed to her to have begun with a "cold" about four months previously.

Examination showed the patient to be of slight build, weighing about 100 pounds (45 Kg.), and to be anemic and poorly nourished. A mass the size of a large English walnut protruded from the left cheek. It was freely movable, and, like all the glandular enlargements, was not tender. Both preauricular glands were visible as well as palpable. The left eyeball seemed abnormally larger than the right, and the lids closed imperfectly. This was due to a smooth pinkish mass, approximately 6 mm. wide and 15 mm. long, lying close to the cornea but not invading it, in the temporal half (fig. 1*A*). Its greatest height above the surface of the globe was about 3 mm., and at the superior ciliary margin it hung over on

the cornea. The bulbar conjunctiva was deeply congested. Near the center of the cornea was a punctate, pitted leukoma 1 mm. in diameter surrounded by an irregular-shaped zone of nebulous infiltrate. This corneal lesion seemed due to the imperfect closure of the lids, there being no history of trauma or corneal disease. The right globe had a growth symmetric with the left but smaller, as it began later (fig. 1*B*). The cornea was clear, and the lids approximated normally. The vision of the right eye was 20/20—, and 20/20 clear with correction; that of the left eye was 20/100 blurred and 20/20— with correction. The media and the fundus of each eye were apparently normal, except for the blur caused by the condition of the left cornea. Nodules were palpable in the superior portions of both the anterior and the posterior cervical chains; the epitrochlear glands were palpable in both elbows, and the inguinal glands were of moderate size. The upper lip was slightly swollen, and some infiltration could be felt. The patient stated that this condition seemed to vary. The air passages were very narrow, and examination of the epipharynx with the pharyngoscope was unsatisfactory because the area was extremely tender. Dr. Warren's roentgenologic report of May 27 stated: "There is no evidence of nodules in the lungs or in the mediastinum, but enlarged glands are seen in the cervical regions."

The case was submitted to the Malignancy Committee of the Hollywood Presbyterian Hospital-Olmsted Memorial, Dr. C. H. Weaver chairman, and the report on a biopsy of inguinal glandular tissue, made by Dr. V. L. Andrews, director of the hospital laboratory, was as follows: "Microsection shows the lymph gland to be completely altered from the histologic point of view. The germinal centers are practically obliterated; lymphoid hyperplasia is present, as well as a considerable increase in the fibrous tissue. The blood vessels and capillaries show thickened, hyaline walls. There are numerous eosinophils and some large cells somewhat resembling Dorothy Reed cells. Occasionally, though rarely, a giant cell with a couple of nuclei is seen. The picture is not typical of Hodgkin's disease, being more that of a chronic inflammatory reaction; yet, with the eosinophils and the large cells, it suggests the probability that the origin was Hodgkin's disease." Examination of the blood on May 11 gave the following values: erythrocytes 4,140,000, hemoglobin 69 per cent, leukocytes 11,000, color index 0.8, polymorphonuclear leukocytes 64 per cent, eosinophils 14 per cent, and lymphocytes 22 per cent. At the same time the Wassermann (Kolmer) and Kahn reactions were negative. The final report of the committee was a diagnosis of Hodgkin's disease. They said: "The mass in the left cheek is thought to be a cyst and not connected with the left parotid gland."

Dr. Warren's treatment was as follows: A series of roentgen treatments was started May 21, with the last treatment on June 24. During this series the patient received in all 3,000 roentgens distributed to the eyes, the left cheek, the two sides of the neck and the groins. She received 1,400 r to the eyes. A second series was started November 1 and finished December 11. In this series she received 2,000 r distributed as before except that she received no treatment to the eyes. Vitamin B₁ was given to counteract nausea. Improvement in all the nodules was observed after the first few treatments, and they gradually disappeared. The second series was given because there was a suspicion of some glandular enlargement, particularly of the inguinal glands. The general condition steadily improved, and the patient gained weight, looked well and stated that she felt well and was strong enough to resume work.

Ten days after the first roentgen ray treatment the ocular lymphoid growths were thinner and somewhat bleached. In another eight days the eyes were markedly better and all the enlarged glands smaller. Nasal obstruction was no longer

felt subjectively, and the pharyngoscope showed an open epipharynx. The improvement was general and constant. Figure 2 shows the condition of the eyeballs on August 24, when on the right all trace of the growth was gone and on the left only a small remnant of light pink, thin tissue remained. The condition of the left cornea was greatly improved, and there was no asthenopia in near work, as there had been previously. Frequent ophthalmoscopic examinations showed no unfavorable changes in the corneas, the media or the fundi. A moderate correction gave comfortable normal vision. By March 21, 1941 the only glandular

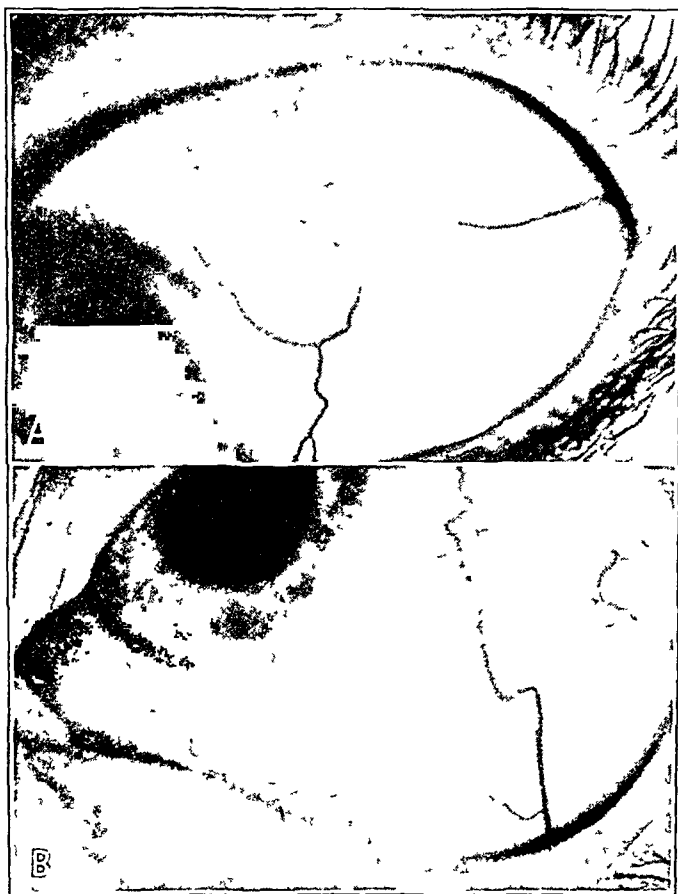


Fig. 2.—*A*, the right eyeball, and *B*, the left eyeball on Aug. 24, 1940, after a series of roentgen treatments.

enlargements palpable were the one in the left cheek, which was small and was felt only on deep palpation; a cordlike condition of the upper anterior cervical chains, small but palpable, which in Dr. Warren's opinion may have been simply a sclerotic, harmless change, and a few small, irregular stained areas on the left globe at the site of the extensive lymphatic infiltration.

In accordance with Dr. MacCallum's hint, previously quoted, an agglutination test for brucellosis was recently made. The reaction was "negative in all dilutions" (Dr. Andrews).

NOTE.—As of Nov. 15, 1941 the globes had remained entirely free from lymphoid tissue, the scleras being white. The vision was normal.

KRUKENBERG'S SPINDLE

A STUDY OF TWO HUNDRED AND TWO COLLECTED CASES

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AND

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Despite the rarity of Krukenberg's spindle in ophthalmologic practice, it has been possible to accumulate a series of 202 cases for review in this study. Ninety-five of these, not previously reported, were collected through a questionnaire addressed to members of the American Board of Ophthalmology in the United States and Canada, and a search of the literature has yielded 107 cases recorded in the forty years since Krukenberg's original description, in 1899.

Although approximately three hundred and fifty physicians and institutions answered the questionnaire, only sixty were able to report cases of Krukenberg's spindle. Thirty-eight described 1 case each; fifteen, 2 cases; four 3 cases. Rosenbaum, of Montreal, contributed 4 cases; Metz, of Cleveland, 5 cases, and Montalvan, of New York city, 6 cases. The details on the 95 collected cases, including one of ours, are shown in table 1. In addition to the contributors who furnished sufficient data on the individual cases for tabulation, four others reported that they had observed 1 case, two had observed 2 cases and fifteen said that they had observed several cases but did not specify the number.

The last comprehensive review of Krukenberg's spindle in English was made in 1930 by Edgerton, who listed 36 cases. In 1934 a review in Italian by Caramazza contained 64 cases. The additional cases in this series of 107 from the literature include those published subsequently and some others, published earlier, which Edgerton and Caramazzo overlooked or omitted.

CLASSIFICATION

In attempting to tabulate and correlate material from so many sources, it is extremely difficult to evaluate the individual criteria and to formulate a definite opinion as to which cases should be included or excluded. Some of the early reports are confusing because the authors were influenced by Krukenberg's theory of the congenital nature of the pigment spindle and by the idea that this manifestation might bear some relation to persistent pupillary membrane.

TABLE 1.—Unpublished

Contributor	Age, Yr.	Sex	Complaint	Type of Error	Refraction and Corrected Vision	Lenses Worn	Spindle	Situation	Direction	Shape
Adelman, B. B., Newark, N. J.	22	♀	Myopia	Myopia	Low refractive error	Unilateral			
	30	♀	Myopia	Low refractive error	Bilateral
Anderson, B., Durham, N. C.	25	♂	Myopia	Corrected vision 20/20	Bilateral
Bankes, C. W., Reading, Pa.	38	♂	"No myopia"	Corrected vision 20/20	Unilateral
Behrens, A., Brooklyn	43	♂	"No myopia"	Unilateral, left
Bell, W. O., Seattle	..	♀	Myopia	Unilateral			
Bloch, F. J., New York	65	♀	Eyestrain	Myopia Hyperopia	+0.5 D. sph. : 20/15 Many years	Unilateral Bilateral	Central	Vertical	Oval
	23	♂	None	Myopia	-3.5 D. sph.					
Blum, H. N., New Orleans	52	♂	Myopia	R. -5.50 D. sph. : 20/70 L. -5.50 D. sph. : 20/30	Bilateral
Bouvy, L. B., La Grande, Ore.	16	♂	Myopia	Bilateral	Oblat
Brannin, Dan, Dallas, Texas	68	♀	Hyperopia	R. +2.00 +0.50 × 90 : 20/25 L. +1.00 +0.50 × 90 : 20/30	Many years	Bilateral	Central	Vertical	Oval
Brown, A. L., Cincinnati	52	♀	Defective vision	Myopia	-2.00 -1.00 × 180 : 20/30	20 yr.	Unilateral	Central	Vertical	Oval
	46	♀	Myopia	Bilateral
Bruner, W. E., Cleveland	41	♂	Emmetropia	Bilateral
Bulson, E., Fort Wayne, Ind.	28	♂	Foreign body in cornea	"No myopia	Unilateral
Campbell, W. E., Jr., Atlanta, Ga.	54	♂	Burning sensation in eyes	Mixed astig- matism	R. -0.50 +2.50 × 45 : 6/10 L. -0.75 +2.00 × 165 : 8/10	9 yr.	Bilateral	Central	Vertical	Oval
Clark, C. P., Indianapolis	45	♂	Myopia	Bilateral
Clement, C. C., Chicago	46	♂	Myopia	Unilateral
	45	♂	Myopia	Bilateral
Cowen, J. P., Chicago	45	♂	Myopia	Bilateral
	31	♀	Poor distant vision	Myopia	R. -1.00 -0.50 × 25 : 20/16 L. -0.87 -0.50 × 175 : 20/16	10 yr.	Bilateral	R. central L. lower half	Vertical	Oval
	50	♀	Blurring of vision and loss of vis- ual fields (4 wk.)	Myopia	R. -5.50 D. sph. : fingers at 3 feet L. -7.00 -1.50 × 30 : 20/50	Bilateral	Central	Vertical	Narrow oval
Culler, A. M., Dayton, Ohio	28	♂	Poor distant vision	Myopia	R. -0.50 -0.5 × 20 : 6/4 L. -0.75 D. sph. : 6/4	No	Bilateral	Central	Vertical	Oval
	28	♂	Loss of vision, right	Hyperopia	L. +0.5 D. sph.	No	Unilateral	Central	Slightly mesial
Ellsworth, E. M., Kingston, Pa.	36	♂	Headache, blurred vision nausea	Mixed astig- matism	R. -1.50 +3.00 × 135 : 6/9 L. -2.00 +4.00 × 15 : 6/9 at exami- nation in 1928 R. -2.00 +10.00 × 165 : 6/9 L. -2.00 +15.00 × 165 : 6/30 at exam- ination in 1935	?	Bilateral	Central	Vertical	Oval
Evans, Odum and Wenans, Youngs- town, Ohio	40	♀	Poor distant vision	Myopia	R. -2.50 -0.50 × 90 : 20/20 L. -2.75 -0.50 × 75 : 20/20	Since child- hood	Bilateral	R. slightly nasal L. slightly temporal	Vertical	Cucum- ber, curved left, both eyes

Size	Densest Pigment	Color of Pigment Spindle	Pigment in Anterior Chamber	Iris Pigment	Inflammation	Pupillary Membrane	Congenital Defects	Acquired Defects	Fields	Comment
.....	Lens opacities	Pigment, anterior surface of lens
.....	Patient unaware of spindle
.....	Detached retina	Patient lost sight of eye
.....	Below center	Brown	No	Brown	No history	None	None	None	Normal	Small choroiditic areas
.....	Glaucoma	
.....	Patient had diabetes mellitus
Large	Center	Golden	No	Gray, with brown specks	No history	None	None	Vitreous opacities	Pigment over anterior capsule; no change in spindle in 10 mo.
.....	Center	Dark brown	No	Blue	None	Glaucoma	Glaucomatous changes	Operation for glaucoma 15 yr. before examination; Wassermann reaction negative
.....	Glaucoma	Operation for glaucoma
.....	Patient referred by Dr. Schonberg
.....	Small nebula	Pigment attributed to foreign body; decreased later
1 x 6 mm.	Center	Brownish	No	Dark brown	Recurrent keratitis	Vertically oval pupils	White specks in cornea	Wassermann reaction negative
.....	Coloboma iris	No change in 5 yr.
.....	Detached retina	Density varied, but pigment spindle remained
.....	Detached retina	
1 x 6 mm.	Top of spindle	Pale tobacco brown	No	Blue-gray	No history	None	2 cilio-retinal arteries, left	None	Patient a physician in good health
4 mm. long	Uniform	Brown, dustlike	No	Light blue	No history	None	None	Glaucoma and detached retina, left	Constriction, left	Detachment of retina in left eye developed after first examination; right retina detached at first examination (Gradle and Snyder)
5.5 x 1 mm.	Lower border of pupil	Brown	No	Light brown	No history	None	None	None	Wassermann reaction negative; patient had pyelitis
4 x 1.5 mm.	Near limbus below	Light brown	No	Light brown	Iritis (8 yr. ago)	None	Synechias, uveal cataract	Light projection limited to 50°	Wassermann reaction negative
3 mm. diameter; 3 mm. from upper and 2 mm. from lower limbus	Lower half	Brown	Brown	None but dacrocystitis, left	None	None	None	Normal	Wassermann reaction negative
R. 6 x 1 L. 5 x 0.75 mm.	Center	Brown	Yes, at times	Brown	No history	None	None	None	Not examined	Patient under care 12 yr.; Wassermann reaction negative; right spindle slightly broader than left

TABLE 1.—*Unpublished*

Contributor	Age, Yr.	Sex	Complaint	Type of Error	Refraction and Corrected Vision	Lenses Worn	Spindle	Situation	Direction	Shape
Fink, W. H., Minneapolis	26	♂	"No myopia"	Unilateral
Fox, C. H., Kearney, Neb.	24	♀	"No myopia"	+ 1 D. cyl. \times 90 : 20/25	Unilateral, left
Hartshorne, I., New York	38	♀	Black specks	Myopia	R. $-0.50 -0.25 \times$ 90 : 20/15+ L. $-0.50 -0.50 \times$ 90 : 20/15+	10 yr.	Bilateral	Central	Vertical	Oval
Hicks, A. M., San Francisco	56	♀	Foreign body, right	Hyperopic astig- matism	Low refractive error corrected to 20/30, both eyes	Bilateral	Central	Vertical	Oval
Hoffman, W. F., Seattle	50	♀	Hyperopia	Unilateral	Central	Vertical	Round oval
Hopkins, G. H., Pueblo, Colo.	48	♀	Poor vision, right	Myopic astig- matism	R. $-2.25 -2.50 \times$ 90 : 1/60 L. $-1.50 -3.00 +$ 2.75 for near \times 90 : 20/25	40 yr.	Bilateral	Central	Vertical
	60	♀	Redness and dis- comfort	Myopia	R. $-6.00 -1.75 \times$ 100 : 20/60 L. $-1.25 -2.00 \times$ 15 : 20/20	28 yr.	Unilateral, right	Central	Vertical
Hosford, G. N., San Francisco	46	♂	"No myopia"	Unilateral
Hughes, W. L., Hempstead, N. Y.	30	♀	Unilateral
	41	♀	Myopia	R. $-1.75 -0.50 \times$ 120 : 20/25 L. $-1.75 -1.00 \times$ 70 : 20/15	Bilateral
Jacoby, M. W., Cleveland	48	♂	Eyestrain	Myopia	R. $-0.50 +1.00 \times$ 5 : 6/4 L. $-0.50 -0.50 \times$ 155 : 6/4	20 yr.	Bilateral	Central	Vertical	Round oval
Katz, D., Hartford, Conn.	24	♀	Myopia	Bilateral
Landesberg, J., Brooklyn	30	♀	Myopia	Unilateral	Vertical
	40	♀	"No myopia"	Unilateral	Vertical
	..	♀	"No myopia"	Unilateral	Vertical
Lemoine, A. N., Kansas City, Mo.	45	♀	"No myopia"	Bilateral
Levitt, J. M., Brooklyn	42	♀	Myopia	-10.00 D. sph., both eyes	Bilateral
McAdams, W. R., Portland, Maine	70	♀	Photo- phobia, headache	Hyperopia	R. $+2.00 +0.75 \times$ 90 — 2 out : 6/9 L. $+2.00 +2.00 \times$ 90 — 2 out : 6/9 — 2	Bilateral	Central	Circular
McMurray, J. B., Washington, Pa.	55	♀	Poor vision	"No myopia"	Vision after cor- rection: R. 20/50 L. 20/15	Bilateral	Central	Vertical	R. wider at lower edge, L. narrow
Mehney, G. H., Grand Rapids, Mich.	33	♀	Myopia	-1.50 D. sph., both eyes	Bilateral
Mengel, W. G., Camden, N. J.	45	Bilateral
Metz, R. B., Cleveland	38	♀	Recurrent lid infec- tion	Hyperopia	Slight refractive error corrected to 6/5, both eyes	No	Bilateral	Vertical	Slightly wider below
	32	♀	Eye fatigue, headache	Compound astig- matism	Slight refractive error corrected to 6/5, both eyes	8-10 yr.	Bilateral	Nasal side of center	Vertical	Band
	41	♂	Discomfort	Myopia	Moderate error corrected to 6/5, both eyes	22 yr.	Bilateral	Central	Vertical	Fusiform
	35	♂	Headache	Hyperopia	Moderate error corrected to 6/5, both eyes	9 mo.	Bilateral	Central	Vertical	Fusiform
	50	♂	Requested refraction	Myopia	Moderate error corrected to 6/5, both eyes	25-30 yr.	Unilateral, right	Central	Vertical	Fusiform

Size	Densest Pigment	Color of Pigment Spindle	Pigment in Anterior Chamber	Iris Pigment	Inflammation	Pupillary Membrane	Con-genital Defects	Acquired Defects	Fields	Comment
.....	None	None		
.....	None	None		
3 × 1 mm.	Center	Brown	No	Brown	No history	None	None	None	Normal	Wassermann reaction negative; patient seen 1927 and 1931; no spindle; first noted 1937; no change since; patient neurotic; endocrine imbalance
2 × 6 mm.	Yellow-brown	No	No history	None	None	None	Not examined	Right eye healed satisfactorily after removal of foreign body
.....	Center	Brown	Blue	No history	None	None	None	Not examined	Spindle showed no change over several years
.....	Center	Brown	No examination	No history	None	None	Hyalitis, both eyes; detached retina, right	R. restricted L. normal	Operation for retinal detachment unsuccessful; vitreous opacities, left eye
.....	Center	Dark brown	No examination	Conjunctivitis, eyelitis (?)	None	None	Glaucoma, bilateral	Normal	Questionable whether recurrent inflammation was eyelitis
.....	None	None	Patient seen only once
.....	None	None	
.....	Lens opacities	L. hyperphoria, 5 D.
5 mm.	Mid-vertical portion	Dark brown	No	Brown	No history	None	None	None	Not examined	
.....	Chronic eyelitis	Patient had attack of chronic eyelitis when first seen
.....	History of eye injury
.....	History of eye injury
.....	History of eye injury
.....	Eyes slightly congested most of the time
.....	Detached retina and hypotony, right	
1/2 cornea diameter	Center	Brownish	No	Blue	None	None	None	None	Normal	Case followed 1 yr.
.....	Brown	Keratitis	Normal	Right eye injured by piece of steel several years earlier
.....	None	None		
.....	None	None		
.....	Brown	No	Gray, with pale brown zones	No history	None	None	None		
R. 4 × 1.5 L. 4 × 2 mm.	Gray, with pigment spots	No history	None	None	None		
.....	Center	Brown	Yes	Brownish gray	No history	None	None	None		
.....	Middle	Brown	Gray edge, brown center	No history	None	None	None		
.....	Middle	Brown	Blue-gray	No history	None	None	None	Spindle appeared 10 yr. after patient first seen, at age 50

TABLE 1.—Unpublished

Contributor	Age, Yr.	Sex	Complaint	Type of Error	Refraction and Corrected Vision	Lenses Worn	Spindle	Situation	Direction	Shape
Montalvan, P., New York	22	♀	Bilateral
	35	♀	Bilateral
	47	♀	Unilateral
	49	♀	Unilateral
Myers, R. W., Worcester, Mass.	63	♂	Unilateral
	65	♂	Unilateral
	47	♂	Myopia	R. —0.50 —1.00 × 100 : 20/25 L. —0.25 —1.25 × 65 : 20/25	25 yr.	Bilateral	Central	Vertical	Oval
Paton, R. T., New York	40	♂	Failing vision	Myopia	R. —8.00 —0.75 × 100 : 20/30—1 L. —8.00 D. sph. : 20/200	Bilateral	Central	Slightly oblique	Oval
Pinkerton, F. J., Honolulu, Territory of Hawaii	35	♂	Reduced vision	Myopia	Moderate refrac- tive error cor- rected to 20/70, both eyes	15 yr.	Unilateral, right	Central	Vertical	Clubbed below
	15	♂	Reduced vision	Myopic astig- matism	Marked refractive error; axis of astigmatism, 90; vision 20/200, both eyes	No	Unilateral, right	Central	Vertical	Oval
	26	♀	Reduced vision, red eyes	Several years	Unilateral, left	Central	Vertical
Pischel, D. K., San Francisco	45	♂	Foreign body	Emmetropia	Bilateral
Place, E. C., Brooklyn	23	♀	Vision after cor- rection 20/20, both eyes	Bilateral	Central	Vertical	Band, wider at center
Reese, A. B., New York	41	♀	Severe headaches	Myopia	R. 0.50 D. cyl. × 180 : 20/15 L. 0.25 D. cyl. × 180 : 20/15	Unilateral, left	Vertical
Reim, Hugo, St. Louis	58	♀	"No myopia"	Bilateral
Robbins, A. R., Los Angeles	33	♀	Loss of vision, scintillating scotomas, chromopsia	Myopia	R. —5.50 D. sph. : 20/25 L. —11.50 D. sph. : 5/200	15 yr.	Bilateral	Midline	Vertical	Spindle
Roberts, W. H., Pasadena, Calif.	42	♀	Poor vision	Myopia	R. —4.50 D. sph. : 6/6 L. —5.50 D. sph. : 6/7	Few mo. as child	Bilateral	Central	Vertical
Rosenbaum, J., Montreal, Quebec, Canada	16	♂	Headaches	Hyperopia	Both eyes +2.50 D. sph. : 6/7	No	Bilateral	Central	Vertical	Irregular
	40	♂	Defective vision	Myopia	Both eyes —1.00 D. sph. : 6/7	No	Unilateral	Central	Vertical	Long and narrow, Irregular
	22	♀	Headaches	Hyperopia	R. +0.75 D. sph. : 6/6 L. +0.50 D. sph. : 6/6	No	Bilateral	Central	Vertical
	20	♀	Headaches	Myopia	Both eyes —1.50 D. sph. : 6/6	5 yr.	Bilateral	Central	Vertical	Barrel- shaped Spindle
Rychener, R. O., Memphis, Tenn.	30	♂	Muscae	Myopia	R. —16.50 D. sph. : 15/50 L. —18.00 D. sph. : 15/50	20 yr.	Bilateral	Central	Vertical
Sherman, A. R., Newark, N. J.	42	♀	Presbyopia	Emme- tropia	No refractive error	No	Bilateral	Central	Vertical	Spindle
	26	♀	Myopia	Both eyes —7.00 D. sph.	Unilateral
	30	♂	"No myopia"	Bilateral
Simmonds, N. T., Alexandria, La.	47	♀	Eyestrain	Myopia	R. —5.25 —0.50 × 82 +1.75 : 6/6 L. —3.50 —1.25 × 112 +1.75 : 6/6	10 yr.	Bilateral	Central	Slightly oblique	Spindle
Somberg, J. S., New York	37	♀	"No myopia"	Bilateral
	17	♂	"No myopia"	Bilateral
Stevenson, W., Quincy, Ill.	45	♂	Slight eyestrain	Hyperopia	Both eyes +0.25 +0.50 × 90 : 20/15	Many years	Bilateral	Central	Vertical	Oval

Size	Densest Pigment	Color of Pigment Spindle	Pig- ment in Anterior Chamber	Iris Pigment	Inflam- mation	Pupill- ary Mem- brane	Con- genital Defects	Acquired Defects	Fields	Comment
.....	Glaucoma	Amblyopia ex anopsia; senile change
.....	Senile change
6 × 0.5 mm.	Center	No history	None	Senile change
2 mm. from lower lim- bus	Senile change
Extended beyond upper and lower lim- bus	Center	Brown	No	No history	None	Slight ectropion uveas	Few small sears of cornea, glaucoma	Scotoma, left; peri- pheral con- traction, left nasal field	Patient had fron- tal sinusitis as a young man; had filtering opera- tions for glau- coma of left eye
1 cm.	Lower part	Brown	Few flecks	Brown	Years ago	None	None	None	Not exam- ined	Wassermann reac- tion negative
2 mm. wide at center	Center	Gray- brown	No	Brown	As child	None	None	None	Normal	Wassermann reac- tion of mother negative
.....	Center	Brown	No exami- nation	Brown	Yes	None	None	Not exam- ined	Examination incomplete; patient seen only once
.....	None	None	Patient a physi- cian in good health
Lower to upper limbus	Center	Brown	No	No history	None	None	None	Not exam- ined	Wassermann reac- tion negative
.....	No history	None	Mitten- dorf dot, right	None	Not exam- ined
.....	None	None	Patient not followed
10 × 1.5 mm.	Center	Brown	Yes	Brown	No history	None	Coloboma of disk, bilateral	Juvenile glaucoma	Marked defects, both eyes	Operations with trephine, with peripheral iridec- tomy, for glau- coma: tension, R. 35, L. 45, before operations
.....	No	No history	None	None	None	Not exam- ined	Patient has not been seen for 7 yr.
2 × 5 mm.	Center	Dark brown	No	Dark brown	No history	None	None	None	Normal	Wassermann reac- tion negative
3 mm.	Center	Brown	No	Brown	No history	None	None	None	Normal	Wassermann reac- tion negative
4 mm.	Center	Dark brown	No	Dark brown	No history	None	None	None	Normal	Wassermann reac- tion negative
.....	Center	Brown	No	Brown	No history	None	None	None	Normal	Wassermann reac- tion negative
7 × 2 mm.	Center	Brown	No	Brown	No history	None	None	None	Normal	Patient of Italian descent; no change in spindle in 1 yr.
1 × 3 mm.	Center	Brown	No	Blue	No history	None	None	None	Normal
.....	Inferior conus	Patient a Negro
.....	Brown	Brown	No history	?	None	None	Not exam- ined
.....	None	None	Patient seen once
.....	None	None	Patient seen once
⅔ of cornea	Center	Dark brown to black	No	Blue	No history	None	None	None	Not exam- ined	Spindle discovered at age 25; patient in good health; Wassermann reac- tion negative

TABLE 1.—*Unpublished*

Contributor	Age, Yr.	Sex	Complaint	Type of Error	Refraction and Corrected Vision	Lenses Worn	Spindle	Situation	Direction	Shape
Thomas, E. R., Dayton, Ohio	29	♂	Myopia	R. $-1.75 -0.25 \times$ 90 L. $-1.50 -0.75 \times$ 90	Bilateral
	63	♂	Myopia	Bilateral
Thomas, Maxwell, Dallas, Texas	32	♂	Sensation of some- thing in the eye	Myopia	R. $-1.25 +0.62 \times$ 18 : 10/10—1 L. $-0.87 +0.50 \times$ 160 : 10/10—1	No	Bilateral	Central	Oblique, upper part to temporal side, both eyes	Narrow oval
	40	♀	Headache, eyestrain	R. $+0.37$ D. cyl. $\times 15$ L. $+0.12$ D. cyl. $\times 165$	No	Unilateral	Central, lower half	Vertical	Oval
	50	♀	Haziness of vision	Hyperopia	R. $+0.50 +0.50 \times$ 35	5 yr.	Unilateral, right	Below center	Diamond shaped
Weeks, J. S., Portland, Ore.	..	♂	Bilateral			
Wetzel, J. D., Lansing, Mich.	50	♂	Unilateral			
	50	♀	Unilateral			
Zentmayer, W., Philadelphia	31	♀	Myopia	Slight refractive error	Bilateral
Zimmerman, J. L., Harrisburg, Pa.	62	♀	Myopia	R. -4.00 D. sph. : 20/70 L. -4.00 D. sph. : 20/25	Bilateral
Zubak, M. F. C., Wheeling, W. Va.	40	♀	Myopia	Unilateral
	40	♀	Myopia	Bilateral

In reviewing cases which had previously been described by other observers, some early authors also excluded from consideration cases in which there was any evidence of inflammation or injury, since they accepted the congenital nature of the origin of Krukenberg spindles, and thus some cases which should have been considered were omitted from later reviews. In including some of these cases in this report, we have been guided by the author's description of the pigment formation in the eye rather than by the causes to which it was attributed. For instance, the case described by Weinkauff was excluded by Edgerton and other authors because the patient had syphilis of two years' duration and also had choroiditis. Since Weinkauff had not examined the patient before he had syphilis, these reviewers felt that the pigmentation could not properly be considered as of "congenital origin." Nevertheless, Weinkauff himself described it as "melanosis of the cornea" of the Krukenberg type. An additional case, described by Stock, is also included here, although it was omitted by Edgerton, perhaps because the pigmentation on the cornea was described as grayish.

For the most part, the opinion of the original observer as to whether the pigmentation should be classified as Krukenberg's spindle has been

Size	Densest Pigment	Color of Pigment Spindle	Pigment in Anterior Chamber	Iris Pigment	Inflammation	Pupillary Membrane	Con-genital Defects	Acquired Defects	Fields	Comment
.....	Paresis of external rectus muscle, right; spindle unchanged over several years
.....	Wassermann reaction negative
R. 6.5 × 2 L. 5.5 × 1.5 mm.	R. Center L. Below center	Brownish	Yes	Brown	Keratitis (3 mo.)	None	None	Nebula at 5:30, 3 mm. from limbus, 1 mm. in diameter	Normal	Wassermann reaction negative
7 × 2 mm.	Margin of pupil	Few specks	No history	None	None	None	Normal	In periphery of fields, 2 mm. white, 360 mm. distance; Wassermann reaction negative
.....	Lower inner part	Yes	Blue	Present in history	None	None	Cataract, detached retina, left	Not examined	Left eye blind after extraction of lens and total detachment of retina; atypical lesion
.....	Yes	None	None	Spindle unchanged for 4 yr.; patient Jewish
.....	None	None	Vision unchanged for 6 yr.
.....	Uveitis
.....	None	None	None

accepted, although a few omissions have been made when the description of the pigmentation seemed too much at variance with the accepted picture of Krukenberg's spindle. On this basis, a case described by zur Nedden as of the Krukenberg type of pigmentation is excluded because he stated definitely that the deposit was not in spindle formation and that it formed a network on the posterior surface of the cornea. Two of the cases described by Waardenburg also were excluded, although 3 others, which were omitted by Edgerton, are included here.

Despite the efforts which have been made in this analysis to appraise both the collected and the reported cases critically, certain inconsistencies and discrepancies are unavoidable because a factor of individual interpretation enters into the diagnosis of Krukenberg's spindle. This is evident both in the questionnaires and in the cases reported in the literature. Some observers with more zeal and imagination no doubt have made a diagnosis of Krukenberg's spindle in cases which more conservative observers would have listed merely as cases of pigmentation of the cornea.

In answering the questionnaire, Waite, of Boston, made a cogent comment on this point: "In our series of 2,002 diabetic patients we

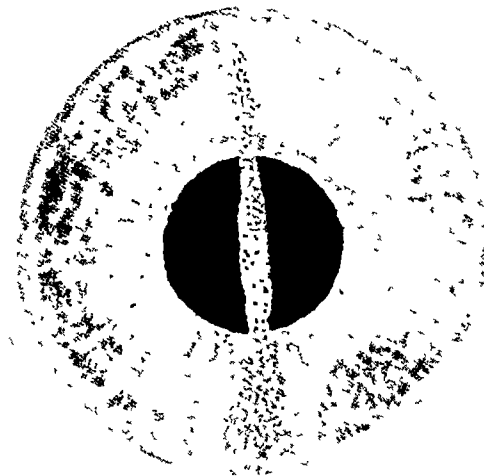
found pigment deposits on the posterior corneal surface in 12 per cent, as contrasted with a 5 per cent incidence in nondiabetic patients of corresponding ages. How many of the deposits could honestly be catalogued as of the Krukenberg type would depend on the imagination and enthusiasm of the observer." Post, of Joplin, also made an interesting reply: "I do not remember having seen a true textbook picture of Krukenberg's spindle. I have seen practically the same formation with the pigment band transverse, and I have seen triangular deposits and a multitude of scattered deposits." From Messenger, of Boston, came the following statement: "I have never seen what I should call a typical Krukenberg spindle. In at least 3 adults (2 women and 1 man), all myopes with some evidence of choroidal disturbance, I have seen a distribution of endothelial pigmentary deposits somewhat suggestive of a fusiform arrangement." In an article by Sallmann on cases from Fuchs's clinic, a similar conservative attitude is evident. In reporting 2 cases of true Krukenberg spindle, he described 6 additional cases of pigmentation of the cornea, 2 of which would possibly have been classified as cases of Krukenberg's spindle by some authors. In 1 of these there was marked dystrophy of the endothelial layer of the cornea, with diffuse pigmentation more marked at the center, and in the other there was a horizontal band of pigmentation in each eye similar to that in the case reported as an instance of Krukenberg's spindle by Krämer.

INCIDENCE

It is impossible to make any estimate as to the incidence of Krukenberg's spindle. The fact that from sixty of the three hundred and fifty ophthalmologists who answered the questionnaire almost as many cases were collected as had previously been reported in the world literature would seem to indicate that this formation is not so rare as previously supposed. Certainly with the use of the corneal microscope, when the condition is watched for it is more likely to be recognized. On the other hand, the condition is not at all common, in view of the relatively large number of cases in which there is some pigmentation of the posterior surface of the cornea. A good many ophthalmologists of wide experience have never seen a Krukenberg spindle. The statement of Post, already quoted, is interesting in this connection. Dimitry, of New Orleans, also made a significant comment: "In the last seven years I have not seen this formation in the largest clinic of the South." Verhoeff replied that he had seen a number of examples but had never reported one and had never recognized the condition microscopically.

TYPICAL KRUKENBERG'S SPINDLE

The typical, or classic, Krukenberg spindle is a narrow or rounded oval of brown pigment, 0.5 to 2.5 or 3 mm. in width and 2 to 6 mm.



A typical Krukenberg spindle.

in length, situated in a vertical line on the posterior surface in the center of the cornea. The pigment is densest at the center, thinning out at the edges, and often has flecks scattered outside the spindle formation. This is the description presented in most of the case reports, although there are some minor variations and a few instances in which the formation was atypical in shape or direction.

In some cases in the series, the spindle was not described but was said to be typical in size, shape and direction. Of the cases in which a definite description was presented, the direction was vertical in 101. In 1 case it was said to be slightly mesial, and in 11 it was oblique. In only 3 was the spindle horizontal or nearly so, and in 2 it was described as curved or arched.

In 94 cases the situation of the spindle was central. It was slightly to the nasal side of center in 10 and to the temporal side in 4. In 7 it was described as below the center of the cornea, and in 1, above the center.

There is more variety in the descriptions of the shape of the formation, but in most cases (in 60) the pigmentation was classified as oval. In 25 it was called spindle shaped, in 8 a narrow oval, in 6 a round oval, in 1 barrel shaped, in another elliptic and in still another diamond shaped. All these descriptions probably fit the same general type of pigment deposition, making a total of 102 cases. In an additional 6 cases the pigmentation was described as like a band or ribbon, possibly wider at the center. Such formations might conceivably be fitted into the classification of oval by some observers. At least two other shapes were described which do not fit readily into the classification of typical. In 6 instances the pigment was said to be broader at the base, more or less in the shape of a pyramid, and in 2 it was described as like a comet, with the pigment thinning and fanning out in the lower portion. In 6 cases it was described as irregular in shape. The last group of cases might be considered questionable, and the pigmentation probably would not be diagnosed as Krukenberg's spindle by some observers.

In 187 cases, a definite statement was made as to whether a spindle was present in one or in both eyes. In 140 cases (74.8 per cent) the condition was bilateral. In 5 it developed in one eye and several months or a year or two later appeared in the other. In 2 it was present first in the right eye, and in 2 the first appearance was in the left eye. In 6 cases comment was made that the spindle was darker in one eye than in the other. In 5 the darker spindle was on the right, and in 1, on the left.

Of the 47 cases in which the spindle was present in only one eye, it was in the left eye in 8 and in the right in 7. In several of the cases

of unilateral involvement, on the posterior surface of the other cornea there was scattered pigmentation which had not assumed a spindle formation.

In 5 instances, the patient had been examined previously by the same oculist with no observation of the spindle. In 1 case, reported by Kayser, the patient was observed routinely for seventeen years, because of megalocornea, before the spindle appeared. In this case it developed first in the left eye and two years later in the right.

In 10 cases comment was made that there was no change in the appearance of the spindle on repeated examination. In several of these operations for cataract or glaucoma were performed without any change in the pigment spindle. On the other hand, in 4 cases the pigment decreased and in 2 there was an increase. Two authors reported that the density of the pigment spindle varied at different observations. The only explanation offered for this change was made in a case by Sommer, who said that the pigmentation became lighter after an Elliot trepanation for glaucoma. In another of his cases, in which an operation for cataract was performed, there was no change in the density of the corneal pigment.

In connection with change in the appearance of the spindle, an allusion made by Lederer is interesting. He stated that in a case reported by Freytag (Lederer furnished no reference) the patient, a man with unilateral myopia, would get transient deep-dotted dark stripes on the cornea when exposed to cold.

ATYPICAL FORMATIONS

In 2 of the cases contributed by Rosenbaum (table 1) the pigment formation was described as irregular. Bietti and also Doggart (table 2) made definite comments that the pigment was not arranged in true spindle fashion. The former said that the pigmentation occupied almost the entire nasal side of the cornea. Doggart did not describe the shape of the pigment formation in his case but stated that it was not arranged spindle fashion, although he reported it as a Krukenberg spindle. Gallenga regarded his case as an atypical instance of Krukenberg's spindle. The pigmentation, he said, was in the form of a ribbon, roughly spindle shaped. The other features which he cited as atypical, however, can scarcely be so regarded. These were the light iris, the depigmentation of the iris, the unilaterality and the youth of the patient (28 years). In one of Koby's cases, the spindle, which was unilateral, was visible only with the microscope and in the other eye the microscope disclosed a few scattered pigment flecks such as are seen in the normal eye.

The case reported by Krämer, which was one of the earliest cases in the literature and has been accepted by all subsequent authors as an instance of Krukenberg's spindle, is atypical in that the pigment band in the cornea lay in a "horizontal direction, with the nasal end broader." Waardenburg's cases, which apparently are similar to this one of Krämer's, have not been so widely mentioned by other authors. In 1 case Waardenburg described the pigment as broader at one end, that is, of V shape. Another similar case, reported by Sallmann and already mentioned, has not been included in the tabulations because the author did not consider it a case of true Krukenberg spindle, although it may belong in this group of atypical cases.

The first case described by Vogt is atypical because the "pigment assumed a mosaic pattern in spindle shape." The author commented that this was the only time in 3,000 slit lamp examinations that he had seen corneal pigment assume a mosaic pattern. This case brings to mind 2 others, in which the pigment was described as a network on the posterior surface of the cornea. One of these was reported in 1900, by zur Nedden, who compared it to Krukenberg's cases but said that the pigment was not in spindle formation. This case has been considered by some authors as an instance of Krukenberg's spindle, but it has not been included in the present tabulation. Another case apparently similar is that described by Shōji. He did not consider the pigmentation to be Krukenberg's spindle, although he commented that the age of the patient, 64 years, and the situation of the pigment, on the posterior surface of the cornea, might suggest it. The pigment was not arranged in a fusiform axis but formed a "network of pigmentation."

STATISTICAL DATA

Complaints.—There are no characteristic symptoms or complaints associated with Krukenberg's spindle. In only a few cases was the complaint which brought the patient to the oculist possibly related to the presence of the spindle. One patient complained definitely of a film over the eye, and 3 complained of black specks or muscae volitantes. In 1 case the complaint was chromopsia and in another scotomas. In still another there was a sensation as of a foreign body in the eye. The symptoms in these cases may have had some relation to the presence of the spindle. In other instances mention was made that the patient was aware of the spindle but this was not the presenting complaint. In 1 instance in which the spindles were bilateral, the patient was aware of some blurring of vision in one eye but not in the other. The great majority of the patients were unaware of the pigmentation in the cornea and it was discovered in the course of examination for other conditions.

Author	Age, Yr.	Sex	Complaint	Type of Error	Refraction and Corrected Vision	Lenses Worn	Spindle	Situation	Direction	Shape
Ascher, 1937	84	♀	Diminution of vision	Myopia	—4.00 D. sph.: 6/24	10 yr.	Bilateral	Spindle
Augstein, 1912	..	♂	Spindle
	Spindle
	Spindle
	Spindle
	Spindle
Bauer, 1931	59	♀	Myopia	R. —12 D. sph.: 2/60 L. —10 D. sph.: 4/60	20 yr.	Central	Vertical	Oval
	31	♀	Disturbance of vision, right (5 days)	Myopia	R. uncertain finger counting, no accom- modation L. —13 D. sph.: 6/18	Bilateral	Central	R. vertical L. oblique, upper part toward tem- poral side	Oval
Bietti,	48	♀	Loss of vision, left	Myopia	R. —6.00 D. sph.: 5/5 L. —10 D. sph.: 5/10	Unilateral, left	Nasal side	Vertical	Roughly oval
Bormacher, 1931	36	♀	Disturbance of vision	Myopia	R. —2.00 D. sph. L. —2.00 D. sph.	Bilateral	Spindle
	42	♀	Chronic con- junctivitis	Emmetropia	Bilateral, right more definite
Butler, 1927	Central	Vertical	Oval
	Bilateral	Central	Vertical	Circular
Caramazza, 1934	60	♀	Failing vision	Myopia	—1.00 D. sph.	Bilateral	Central	Vertical	Elliptic
	51	♀	Failing vision	Myopic astigmatism	—2.00 D. sph.: S/10	Bilateral	Spindle, more defi- nite in left eye
Cardell, 1926	30	♀	Myopia	R. —10.00 D. sph. L. —20.00 D. sph.	Bilateral	Central	Oval
Cardell, 1930	42	♂	Diminished vision	Myopia	R. —2.25 D. sph.: 6/6 L. —2.75 D. sph.: 6/9	Bilateral	2 mm. be- low center of cornea	Oblique	Oval
Cavara, 1929	54	♀	Myopia	R. —12 —0.50 × 180: 5/15 L. vision 1/50	Bilateral	Central	Vertical	Oval
Doggart, 1930	42	♂	Myopia	Vision after correc- tion 6/6	Bilateral	Central	Vertical	Not spindle
Edgerton, 1930	38	♂	Pterygium	Hyperopia	Vision after correc- tion 6/5	No	Bilateral	Central	Vertical	Oval
Ezell, 1922	60	♂	Burning, eye fatigue, headache	Myopia	Vision after correc- tion 20/70	More than 15 yr.	Bilateral	Central	Oval
Focosi, 1933	54	♂	Progressive myopia	Myopia	R. —10 D. sph.: 5/7.50 L. —14 D. sph.: 5/30	Many years	Bilateral	Central	Vertical	Round oval
	62	♂	Reduction of vision	Myopia	R. —2 D. cyl. × 90: 2/40 L. —0.5 D. cyl. × 90: 2/40	Bilateral	Central and medial	Arched and ver- tical at 5 o'clock	Comet
	41	♂	Short sight	Myopia	R. —17 —0.75 × 90: 5/7.50 L. —17 —0.75 × 90: 5/7.50	Bilateral	Central	Vertical	Oval

Size	Densest Pigment	Color of Pigment Spindle	Pigment in Anterior Chamber	Iris Pigment	Inflammation	Pupillary Membrane	Con-genital Defects	Acquired Defects	Fields	Comment
.....	No	Brown, edge, de-pigmented	Cortical opacities of lens	Normal	Under observation until death, at 96; vision remained unchanged; no increase in intraocular tension
4 × 15 mm.	Center	Reddish brown	Brown, edge de-pigmented, pigment flecks	Irido-cyclitis	Atrophic chorioid, slight arcus senilis	Patient a nervous, obese woman under observation more than 20 years before spindle discovered
.....	Center	Brown	Brownish gray	Choroiditis	R. vitreous opacities, small conus, pale fundus; L. conus choroidal atrophy	No one else in family had myopia or any eye trouble; iris pigment not rarefied on edge
.....	Brown	Yes	Brown	No history	None	Annular pigment of lens	Pigment distribution somewhat atypical; occupied almost entire nasal side; area smaller 6 months later
.....	Flecked	No history	None	Detached retina	
.....	Flecked	No history	None	
.....	Center	Brown	Case of Mr. Viner
.....	Case of Mr. Clegg
3.5 × 2 mm.	Center	Reddish brown	Dark, some pigment spots	Patient had severe myocarditis
4 × 2 mm.	Center	Reddish to chocolate brown	No	Dark, slight pigmented dystrophy	Incipient cortical opacities, left; fluid vitreous; degeneration of hyaloid arteries	Wassermann reaction negative; one daughter died of tuberculosis; patient had pleurisy 3 years earlier and had scars at site of glands in neck
1.5 × 3 mm.	Center	Brown	Gray	Choroidal atrophy, left	
4 × 2.5 mm.	Center	Russet brown	Left eye	Brown	No history	None	Pigment scattered throughout cornea	Patient had had a blow on the left eye
4.5 × 2.5 mm.	Center	Dark brown	Few specks	Brown, de-pigmented edge, flecks	Small residue, pigmented slightly	Detached retina, left; annular pigmentation of lens; choroidal atrophy; vitreous exudates	
Below upper border to lower limbus	Reddish brown	Yes	Flecks of pigment	Atypical shape; "not arranged spindle fashion"
3.5 × 1 mm.	Center	Golden brown	Brown	No history	None	None	None	Normal	Wassermann reaction negative
.....	Center	Brown	Brown	No history	Contracted above and below	
.....	Dark brown	No	Dark brown	No history	None	Corneal scars, pigmentation in posterior part of lens	Normal	Corneal injury 1920; staphyloma, right fundus; pigment dystrophy; Wassermann reaction negative
.....	Brown	Yes	Brown, flecked	Annular pigmentation of lens	Wassermann reaction negative; patient had tuberculosis
3 × 1.5 mm.	Brown	Yes	Brown	Annular pigmentation of lens	Normal	Wassermann reaction negative; Pirquet reaction positive

TABLE 2.—Published

Author	Age, Yr.	Sex	Complaint	Type of Error	Refraction and Corrected Vision	Lenses Worn	Spindle	Situation	Direction	Shape
Focasi, 1933 —continued	41	♀	Marked loss of vision keratocon- junctivitis	Myopia	R. —10 D. sph.: 1/40 L. —11 —2.00 × 90: 5/15	Not worn before	Bilateral, left less pronounced	Central	Vertical	Spindle
Ford, 1919	42	♀	Slight dis- charge from eyes and presbyopia	Myopia	Vision after correc- tion 5/9	Not worn before	Bilateral	Central	Vertical, curved in slightly
(Holmes- Spicer)	30	♀	Bilateral	Central	Vertical
	26	♂	Bilateral	Central	Vertical
Friedman, 1929	32	♂	Myopia	Vision after correc- tion 6/8	Bilateral	Central	Oblique 15 degrees	Oval
Gallenga, 1932	28	♂	R. motion at 2 meters L. 10/10	Unilateral, right	Eccentric	Vertical	Ribbon, roughly spindle- shaped
Gifford, 1926	31	♀	R. 20/40+3 L. 20/20—3	Bilateral	Central	Oval
Goar, 1928	40	♂	Poor vision	Myopia	R. —0.75 —1.00 × 50: 20/20 L. —1.50 D. sph.: 20/20	Bilateral	Nasal to center	Vertical	Oval
Greeves, 1931	62	♀	Pain in eye	Unilateral, later bilateral	Central	Oval
Hanssen, 1923	..	♀	Bilateral	Central	Oval
	..	♀	Bilateral	Circular
Hega, 1938	26	♂	Double vision	Emme- tropia	R. —0 D. sph.: 20/20 L. —3 D. sph.: 20/20	Bilateral	Central	Vertical	Oval
von Hess, 1911	59	♀	Myopia
Holloway, 1910	32	♀	Pain in eyes	Hyperopia	Vision after correc- tion: R. 6/5, L. 6/4	8 yr.	Bilateral	External to center, left	Vertical	Oval
	32	♀	Eyestrain	Myopia	R. 6/9, with correction 6/6 L. 6/7.5, with correction 6/6	10 yr.	Bilateral	Central	Vertical	Oval
	40	♀	Poor vision	Myopia	R. 6/22 × 165, with cor- rection 6/6 L. 6/45 × 15, after cor- rection 6/5	25 yr.	Bilateral	Nasal to center	Vertical	Oval
James, 1927	63	♀	Disturbance of vision	Myopia	R. —14 D. sph. L. —10 D. sph.	36 yr.	Unilateral	Nasal to center	Vertical and hori- zontal	Oval
Kayser, 1929 and 1938	23	♂	Film over eye	Myopia	Both eyes —2.75 D. sph.: 6/8	15 yr.	Unilateral, left; 2 yr. later in right also	Central	Vertical	Oval
Koby, 1927	44	♀	Iritis	Emme- tropia	R. 6/8, L. 6/12	No	Unilateral, right	Above and outside center	Vertical	Fusiform
	29	♂	Eyestrain	Myopia	Unilateral, right	Central	Vertical	Wider at base

Size	Densest Pigment	Color of Pigment Spindle	Pigment in Anterior Chamber	Iris Pigment	Inflammation	Pupillary Membrane	Congenital Defects	Acquired Defects	Fields	Comment
3 mm. in length	Brown	Brown	Keratoconjunctivitis	Corneal scars	Periphery normal, central scotoma	This patient only one in series without pigmentation of lens
.....	Brown	No history
.....	Sore eyes in childhood	Brother had interstitial keratitis; no sign of syphilis in patient
$\frac{2}{3}$ corneal diameter	Center	Chocolate brown	Bluish gray	No history	Right eye	Normal
.....	Center	Brown	Light blue, white spots on edge	No history	Residual traces both eyes	Leukoma, right eye	All tests gave negative results except to show tuberculosis; case atypical in several ways; right pupil almost covered
.....	Center	Brown	No history
.....	Center	Chocolate brown	Bluish gray	No history	None
.....	Cupped disk, glaucoma	Second spindle appeared 3 years after first; practically no vision in eye with glaucoma
.....	No history	None	None	Postmortem examination showed much pigment degeneration; patient had not been conscious of spindle
5 × 2 mm.	Center	Brown	Brown	No history	None	None	Diplopia	R. normal; L. contracted	Scattered pigment throughout cornea; imbalance of ocular muscles; patient had dementia praecox
.....	Incipient cataract	Patient had diabetes
2.5 × 1 mm.	Center	Brown	Dark brown	No history	None
3 × 1 mm.	Center	Brown	Bluish gray	No history	None
3 × 1 mm.	Center	Brown	Bluish gray	No history	None
.....	Center	Brown	No history	None	Large myopic crescent	Cataract
.....	Center	Brown	No pigment specks in iris	No history	Megalo-cornea	Arching of cornea, similar to arcus senilis, developed at age 10	Patient under observation many years before spindle appeared. died $4\frac{1}{2}$ years later; pathologic examination showed degeneration of retinal layers of iris pigment
$\frac{1}{4} \times 2$ to 3 mm.	Center, below center of cornea	Brown	Brown	Iritis	Spindle appeared 4 months after iritis, first in left and then in right eye
$\frac{1}{4} \times 2$ to 3 mm.	Center	Brown	Brown	No history	Fine scattered pigment of cornea at first; assumed spindle shape $1\frac{1}{2}$ years later

Author	Age, Yr.	Sex	Complaint	Type of Error	Refraction and Corrected Vision	Lenses Worn	Spindle	Situation	Direction	Shape
Koby, 1928	46	♀	Myopia	Myopia	Bilateral	Central	Inclined slightly to temporal side	Long oval
	22	♀	Myopia	Myopia	Since childhood	Unilateral	Central	Vertical	Spindle
	52	♀	Myopia	Myopia	15 yr.	Unilateral	Central	Vertical	Rounded spindle (roughly)
Korobova, 1929	50	♂	Bilateral	Central	Vertical	Oval
Krämer, 1906	63	♀	Poor vision	Hyperopia	R. 5/18, +1.25 D. cyl. × 10: 5/6 L. 5/12, +1.0 D. cyl. × 10: 5/8 With lenses, both eyes 5/5	Bilateral	Central	Horizontal	Roughly oval
Kraupa, 1917	56	♀	Myopia	—15 D. sph.	Bilateral	Central	Vertical	Oval
	60	♀	Myopia	Bilateral	Central	Vertical	Oval
	60	♀	Myopia	Unilateral, right	Central	Vertical	Oval
Krukenberg, July 1899	45	♀	Myopia	—9 D. sph.	Bilateral	Central	Vertical	Oval
Krukenberg, December 1899	..	♀	Myopia	—1 D. sph.; vision after correction: L. 5/5, R. 5/8	Bilateral	Central	Vertical	Oval
	..	♂	Myopia	R. —5.0 —0.75 × 45: 1.0 L. —6.6 D. sph.; amblyopic	Bilateral	Central	Vertical	Oval
Lasky, 1937	37	♀	Myopia	R. 15/200; —3.50 —1.00 × 120: 20/20 L. 15/200; —3.50 —0.75 × 60: 20/20	Bilateral	Central	Vertical	Oval
	36	♂	Emmetropia	Vision 20/20 both eyes	Bilateral	Central	Vertical	Conical, larger at base
	32	♂	Myopia	R. —4.50 D. sph.: 20/20 L. —4.87 D. sph.: 20/20	Bilateral	Central	Vertical	Oval
	39	♂	R. 20/50; +1.00 —3.00 × 15: 20/30 L. 20/50; +1.00 —3.00 × 150: 20/30	Bilateral	Vertical	Spindle
	23	♀	Eyestrain	Emmetropia	Vision 20/20 both eyes	Bilateral	Below pupils
Lederer, 1930	37	♀	Loss of vision	Myopic astigmatism	R. —0.00 D. sph.: 5/8 (?) L. —5.00 D. sph.: 6/8	Bilateral	Central	Vertical	Thick stripe
Mauksch, 1925	21	♂	Falling vision	Myopia	R. —7.00 —3 × 30: 6/9 L. —7.00 —3.00 × 30: 6/12	Several years	Bilateral, right more marked	Central	Vertical	Band
	21	♂	Perforating injury, right	Severe myopic astigmatism	Bilateral	Central	Vertical	Band

Size	Densest Pigment	Color of Pigment Spindle	Pigment in Anterior Chamber	Iris Pigment	Inflammation	Pupillary Membrane	Congenital Defects	Acquired Defects	Fields	Comment
2 to 3 × 1 to 2 mm.	Brown and gray	No	Gray-brown, brown flecks	Annular pigmentation of lens	Senile depigmentation of iris; some depigmentation of fundus
5 × 3 mm.	Center	Brown	Light brown, no depigmentation	Some residue, left	Some pigmentation of posterior part of lens	Spindle clear with naked eye, right; grayish dust, cornea, left, disk shaped under microscope
Small	Gray-blue	Vitreous opacities, both eyes	Depigmentation of fundus, but not of choroid; pigment flecks visible microscopically, left
.....	Center	Brown	Uveitis	Cataract	Spindle first in right eye; 7 months later in left
.....	Border	Brown	No	Steel gray	No history	None	Bilateral optic atrophy	Atypical formation; horizontal, nasal end blunter than temporal; 2½ times as long as wide
.....	Center	Brown	Brown, pigment flecked	No history	None	Nebula, left cornea	Detached retina, left	
.....	Center	Brown	Brown	No history	None	Acute glaucoma	
.....	Center	Brown	Brown flecked, right; green, left	No history	Pigment flecks, anterior capsule of lens
4 × 3 mm.	Center	Brown	Brown	No history	None	Posterior staphyloma	Patient had had nephrectomy and was being treated for nervousness; anterior chamber deep
.....	Center	Brown	Brown, greenish edges	No history	None	Vitreous opacities	Nervous patient
3.5 × 4.5 mm.	Center	Brown	Brown	No history	None	Glaucoma simplex	Had squint in youth; left eye amblyopic; nervous patient
4 × 2 mm.	Center	Brown	No	Brown, flecked	Both parents myopic; patient myopic since childhood; had had scrofula and otitis media
R. 5 × 3 mm.; L. half as large	Center	Brown	No	Brown	Had sinus disease, tuberculosis, arthritis and 8th nerve deafness
4 × 2 mm.	Center	Brown	No	Brown	Bilateral arcus senilis	Patient an engineer; had worked before electric furnace 1 year
4 × 2 mm.	Center	Brown	No	Brown	None	None	Lens opacity, left	Normal	Eyes large, buphthalmic; sclera blue tinged; anterior chamber deep
2 × 1 mm.	Brown	Brown	No history	None	Pigmented anterior capsule, left lens	Pigmentation not in definite spindle; regarded as developing spindle
R. 5 × 1.5 mm. L. 4 × 1.5 mm.	Center	Brown	No	Brown, flecked	Pigmented anterior capsule of lens	Besides spindle, an uneven broad pigment band on peripheral part of cornea, near limbus; brother myopic, but had no spindle
.....	Center	Brown	Yes	Gray-blue, brown flecks	No history	Embryonal cataract	Annular pigmentation of lens	Atrophic iris; inverse retinal vessels; pigment somewhat denser in 6 months
.....	Center	Brown	Yes	Gray-blue	No history	Embryonal cataract, inverse retinal vessels	Patient twin brother of preceding patient

TABLE 2.—Published

Author	Age, Yr.	Sex	Complaint	Type of Error	Refraction and Corrected Vision	Lenses Worn	Spindle	Situation	Direction	Shape
Mills, 1913	Bilateral	Central	Vertical	Oval
Oeller, 1903										
Peter, 1927	54	♀	Hyperopia	Bilateral	Central	Vertical	Oval
Peters, 1909										
Pincus, 1939	26	♀	Headaches	Myopia	R. -4.00 D. sph.: 6/21 L. -3.00 -2.00 × 180: 6/21	17 yr.	Bilateral	Central	Vertical	Fusiform
Post, 1930	36	♀	Myopia	R. 18/20, corrected to 20/12 L. 18/48, corrected to 20/12	Bilateral	R. 100° L. 100°	Vertical	Oval
	66	♀	R. hand movements at 5 ft.; L. fingers at 1 ft.; vision after cor- rection 18/240	52 yr.	Bilateral	Vertical	Oval
Puglisi-Duranti, 1935	53	♀	Decreased vision, especially left	Hypermetropia	1/10, + 2 D. sph.; 10/10 L. 7/10, + 2 D. sph.: 10/10	Unilateral, right	Central, slightly nasal	Slightly oblique	Fusiform
	53	♀	Failing vision	Hypermetropia	R. 3/10, +4.5 D. sph.: 10/10 L. 3/10, +4 D. sph.: 10/10	2 yr.	Bilateral	Central	Vertical	Fusiform
	44	♀	Myopia	R. -16.00 D. sph. L. -18.00 D. sph.	Bilateral	Central	Vertical	Oval
Sallmann, 1926	42	♀	Failing eyesight	Myopia	R. -18.00 D. sph.: fin- gers at 3.25 meters L. -14 -3 × 180: 5/18	Unilateral, left	Central	Vertical	Spindle
	49	♂	Myopia	R. -2.5 -1.5 × 180: 5/8 L. -2.5 D. sph.: 5/6 (?)	Bilateral	Central	Vertical	Spindle
Schuster, 1930	..	♀	Conjunctivitis	Myopia	R. -13 D. sph.: fin- gers at 1 meter L. -12 D. sph.: 5/20	Bilateral	Central	Vertical	Oval
Seissiger, 1926	68	♀	Myopia	R. -16.0 D. sph.: fingers at 2 meters L. -11.0 D. sph.: fingers at 3 meters	Bilateral	Central	Oblique	Spindle, wider at base
	39	♀	Hyperopia	R. +5.0 D. sph.: 5/4 L. +5.0 D. sph.: 5/5	Bilateral	Central	Oblique	Spindle
	64	♀	Myopia	R. 5/20, -1.25 D. sph.: 5/7 L. 5/10, -1.0 D. sph.: 5/5	Bilateral	Central	Oblique	Comet
Sommer, 1935	31	♀	Conjunctival disease	Emmetropia	Vision, both eyes: 6/6	Bilateral	Central	Vertical	Oval
	69	♀	Myopia	Myopia of more than 5 D., vision after cor- rection: R. -0.9, L. -0.8	Bilateral	Central	Vertical	Oval
	61	♂	Failing vision	R. +1.0 D. sph.: 5/20 L. +1.0 D. sph.: 1/10 eccentric	Bilateral	Central	Vertical	Oval
Springob, 1939	42	♀	Myopia	-6.00 D. sph.	Bilateral	Central
Srinivasan, 1930	27	♀	Occipital headache, right	R. 6/60, -1.0 +3.0 × 90: 6/9 L. 6/18, +0.5 D. cyl. × 180: 6/6 partly	Bilateral	Central	Vertical	Oval

Cases—Continued

Size	Densest Pigment	Color of Pigment Spindle	Pigment in Anterior Chamber	Iris Pigment	Inflammation	Pupillary Membrane	Congenital Defects	Acquired Defects	Fields	Comment
.....	Center	Brown	No history					
Does not extend to limbus	Center	Brown	No history	None				
4 × 1 mm.	Center	Brown, dustlike	No	Brown, pigment flecks in crypts	Interstitial keratitis	None	Corneal opacities	Patient Italian; Wassermann reaction positive on one occasion; slight ptosis of lids; infected tonsils
3 mm. wide	Center	Brown	Brown	No history	None	None	Normal	
.....	Center	Brown	Brown	Yes	None	None	Cataract		
3 × 1.5 mm.	Center	Reddish brown	Few specks	Darker in eye with spindle	No change in 9 mo.; ovaries had been removed 20 yr. before; posterior synechia of iris
4 × 2 mm.	Red-brown	Some depigmentation of border	No history	Senile gerontoxon, slight sclerosis of lens	Slight exophoria
R. 3.5 × 2 L. 4 × 2.5 mm.	Center	Red-brown	Yes	Detached retina, left; lens opacities		
.....	Center	Dark brownish red	Myopic changes in fundus
.....	Dark brown	Optic atrophy	Had syphilis 25 years before
.....	No	Atrophic, some pigment flecks	Beginning cataract	Myopic changes in fundus
0.75 × 1.5 mm.	Outside length	Brown	Gray-brown, pigment flecks, iris atrophic	No history	Right eye	Cataracts, vitreous opacities, posterior staphyloma	Blood pressure 200/90; 41 relatives examined, no spindle; urine normal
4 × 1.5 mm.	Outside	Red-brown	Yes, right eye	Dark brown, no atrophy	Both eyes	Normal	Neurasthenic; brown pigment ring 1 mm. total circumference of limbus
4 × 1.5 mm.	Outside	Brown	No	Gray-brown	Incipient cataract, right	Mother of preceding patient; no general disease; no pigment of corneal periphery
.....	Center	Dark brown	No	Gray-blue pigment flecks	Conjunctival inflammation	Pigment darker after 4 months and accompanied by pigment ring on limbus; father had corneal pigment
.....	Center	Dark brown	No	R. cataract L. aphakia	Spindle not affected by cataract removal; 4 children and 2 grandchildren free from eye changes
.....	Center	Brown	Pigment flecks	Glaucoma	Spindle lost some color after Elliot trepanation
.....	No history	Had film over right eye from pigment spindle, 3 years; light pigment in left eye 4 months
3.5 × 1 mm.	Brown	No history	White fibrous scar, right fundus; patient had had three abortions, no children; pyorrhea and irregular teeth

Author	Age, Yr.	Sex	Complaint	Type of Error	Refraction and Corrected Vision	Lenses Worn	Spindle	Situation	Direction	Shape
Stock, 1901	60	♂	Myopia, poor vision	Myopia	R. —15.0 D. sph.; fingers at 1.5 meters L. —8.0 D. sph.; fingers at 4 meters	Bilateral	External to center, left; central, right	Vertical	Oval
	40	♀	Extremely poor vision	Myopia	R. —18.0 D. sph.; 6/18 L. —18.0 D. sph.; fingers at 1 meter, eccentric	Bilateral	Central	Vertical	Oval
Strebel and Steiger, 1915	69	♀	Myopia	—25.0 D. sph.	Bilateral	Central	Vertical	R. irregular L. oval
	..	♀	Myopia	R. —12.0 D. sph. L. —19.0 D. sph.	Bilateral	Central	Vertical	Irregular ovals
	Myopia	Bilateral	Central	Vertical
	Myopia	Bilateral	Central	Vertical
	Bilateral	Central	Vertical
Tassman, 1930	36	♀	Pain in eyes	Myopia	High degree of myopia, vision after correction 5/40 both eyes	Yes	Bilateral	Central	Vertical	Oval
Thomson and Ballantyne, 1903 and 1927	22	♀	Myopia	Vision after correction 6/9	Bilateral	Central	Vertical	Comet
Tweedie, 1911	25	♂	Myopia	Mild myopia, vision after correction 6/6 both eyes, axes of astigmatism 180 and 97.5	Bilateral; smaller and lighter, left	Internal to center	Vertical	Oval
Vogt, 1921	68	♀	Myopia	—4.0 D. sph.	Bilateral	Central	Vertical	Spindle
	38	♂	Myopia	R. —7.0 —0.5 × vertical: 0.7 L. —6.0 —.0 × vertical: 0.7	Bilateral	Central	Vertical	Spindle
	35	♀	Emmetropia	R. 6/8 L. 1 without glass	Unilateral, left	Central	Vertical	Oval
	48	♀	Myopia	R. weak 1, —1.0 —0.5 L. 6/8, —1.25 —0.5	Bilateral, left darker	Central, right; 0.5 mm. nasal, left	Vertical	Spindle
Waardenburg, 1915	43	♀	Slight myopia	—0.75 D. sph.: 6/6	Bilateral	Central	Slightly nasal	Comet
Waardenburg, 1918	38	♀	Emmetropia	Unilateral, left	Horizontal
	54	♀	Hyperopia	R. +1.75 +1.0 × vertical: 5/10 L. +1.5 +0.75 × 10: 5/10	Below center	Mainly horizontal	V form,
Weinkauff, 1900	60	♂	Poor vision	Myopia	R. —2.5 D. sph.: 5/15—10 L. —2.0 D. sph.: 5/20	2 yr.	Bilateral	Central	Vertical	Oval
Záhoř, 1931	..	♀	Myopic astigmatism
	..	♂	Hyperopic astigmatism
Zentmayer, 1935	16	♂	Distant vision poor	Myopia with astigmatism	R. —0.25 —1.50 × 15: 6/7.5 (?) L. —0.75 —2.00 × 165: 6/7.5	Bilateral	Midline, lower half of cornea	Vertical	Oval
(Friedenwald)	..	♀	Spots, headache, worse at night	20/30, corrected to 20/20	Bilateral	Vertical

Size	Densest Pigment	Color of Pigment Spindle	Pigment in Anterior Chamber	Iris Pigment	Inflammation	Pupillary Membrane	Congenital Defects	Acquired Defects	Fields	Comment
3 to 4 × 2 mm.	Center	Reddish brown	Brown	No history	None	Incipient cataract, vitreous opacities, myopic fundus		
.....	Center	Gray	Gray	No history	Questionable				
.....	Brown	Depigmentation of edge	Vitreous opacities, atrophic fundus		
.....	Brown	No change	Patient daughter of preceding patient
.....	Megalocornea			
3 × 1 mm.	Center	Brown	Brown	No history; choroiditis present	None	None	Vitreous opacities, choroiditis	Wassermann reaction positive
.....	Center	Chocolate brown	No history	None	Partial coloboma of disk			
2.5 × 3 mm.	Center	Yellowish brown	Brown	No history	None	Nebula, right cornea	Nystagmus on movement to left	Patient unaware of opacity in left but aware of it in right eye
1.5 × 3 to 4 mm.	Yellowish brown	Brown	Cataract	Pigment assumed mosaic pattern in spindle shape; not changed by cataract operation
1 × 3 to 4 mm.	Center	Light brown	Blue-gray and brown-gray, pigment flecks	None	Vision unchanged for 6 yr.; extensive degeneration, iris pigment
1 × 3 to 4 mm.	Brownish gray	Blue-gray, brownish flecks, left	Few isolated pigment flecks, right cornea and iris; patient weak and anemic
R. 1 × 2.5 L. 1.25 × 3 mm.	Brown	Brown with pigment scattering						
2.5 mm. wide	Center	Brown	Gray	Cataract	Some pigment in retina
0.5 mm. wide	Brown						
.....	Brown	Brown	Convergent strabismus	Cloudiness at periphery of lens		
R. 2 × 0.75 L. 4 × 0.75 mm.	Center	Dark brown	Dark brown	Choroiditis	Vitreous opacities	Patient treated for syphilis for 2 yr.; pigment on Descemet's membrane in spindle form
.....	None	Central chorioretinitis		
.....	Atrophy of iris	None				
4 × 1 mm.	Brown	Annular pigmentation of lens		
.....	Brown	Aqueous filled with pigment granules	Brown	Yes	Wassermann reaction positive; patient a Negress; spindle disappeared after 1 yr., leaving few pigment granules on cornea

The largest number of patients consulted the oculist because of symptoms related to refractive errors. Poor vision was complained of by 36, eyestrain by 11, headache by 18, near-sightedness by 9, presbyopia by 3 and photophobia by 1. Four others came requesting refraction, and it may be assumed that they had suffered from some symptoms of eyestrain. One patient's complaint was of double vision. Four patients were seen because of a foreign body in the eye and 9 because of inflammation of the lid, conjunctiva or eyeball. Pterygium brought 1 patient to the ophthalmologist. Other patients were seen because of various conditions, such as detached retina, cataract, glaucoma and opacities of the vitreous.

Myopia.—Myopia is the most consistent finding, although Krukenberg's spindle has been observed frequently in hypermetropic or emmetropic eyes. All the authors who have written on the subject have stressed that the preponderant number of patients are myopic. Krukenberg in his original report noted that all 3 of the patients he described were myopic and of highly nervous temperament. Of the series of cases collected from the literature and the questionnaires, the refraction was not given in 36. Of the remaining 166, the patient was myopic in 116 (69.8 per cent), hypermetropic in 22 and emmetropic in 11. In 13 the person who answered the questionnaire stated merely that the patient was not myopic, without saying whether the vision was hypermetropic or normal. These cases have been characterized "no myopia" in the table. In 4 cases the refractive error was mixed astigmatism.

It is interesting to note that in 33 cases specific mention was made that corrective lenses had been worn for ten years or more, and in an additional 10 cases glasses had been worn for varying periods less than ten years. In 14 cases the comment was made that lenses had not been worn previously. The remainder of the authors and contributors did not mention whether the patient had worn lenses. Nevertheless, the fact that in 43 cases, or nearly one fourth of the entire series, the patient had had visual difficulties requiring correction for a considerable period may be significant.

Thorough analysis of the data on cases previously reported and those collected from the questionnaires failed to reveal why this particular pigmentary disturbance of the posterior surface of the cornea occurs preponderantly in patients with myopia. Numerous theories have been advanced, but none offers a completely satisfactory explanation. Whether some of the newer ideas regarding the effect of dietary and endocrine factors on the production of myopia will shed some light on the subject remains to be disclosed by future investigations.

Age.—Almost half (45.1 per cent) of the patients in this collected series were between 30 and 50 years of age. Fifty patients were from

40 to 50, and 41 were from 30 to 40. Krukenberg's spindle was observed in 5 patients less than 20 and in 29 patients between 20 and 30. Fifty patients, approximately 25 per cent, were more than 50. Twenty-four were from 50 to 60, 24 from 60 to 70 and 1 each in the eighth and ninth decades. The age of 27 was not stated. In the 175 cases in which the age was furnished, the percentage distribution according to decades was as follows: second, 2.8 per cent; third, 16.6 per cent; fourth, 23.4 per cent; fifth, 28.6 per cent; sixth, 13.7 per cent; seventh, 13.7 per cent; eighth, 0.6 per cent, and ninth, 0.6 per cent.

Sex.—The proportion of females was slightly higher in the cases which have been published than in the collected cases. In the cases gathered from the literature there were 30 males, 64 females and 13 patients whose sex was not recorded. In the 95 unpublished cases, there were 41 males and 53 females and 1 case in which the sex was not mentioned. In the 188 cases, published and unpublished, in which the sex was reported, 37.7 per cent of the patients were male and 62.3 per cent female. In the series of cases previously published, the ratio of females to males was 68 to 32. From these data it is seen that Krukenberg's spindle is encountered approximately twice as frequently in women as in men. It is interesting, however, and perhaps significant, that in the younger patients, that is, those less than 30, the ratio of males to females was approximately reversed. Of 34 patients in this age group, 21 were males and 13 females. Thus the ratio of males to females was 62 to 38. This fact considered, the proportion of females in the older group is even higher than the two thirds which represents the group as a whole.

A number of authors have commented on the greater susceptibility of women to this condition but have offered no satisfactory explanation. Koby said that it may be due to the greater susceptibility of women to uveitis and cited the appearance reported by Strebel and Steiger, Vogt and Seissiger of the spindle in mothers and daughters as evidence that it might be sex linked. There is little or no evidence in the data on the individual cases that would implicate a female endocrine disturbance in the causation of Krukenberg's spindle. In 1 case mention was made that the ovaries had been removed a number of years previously, in 1 there had been three abortions and in another there was said to have been an endocrine imbalance. In addition, there were 5 cases in which hysteria or neurotic tendencies were recorded. These few observations are of no significance statistically, and probably are merely coincidental.

Color of Iris.—Krukenberg's spindle occurs more frequently in persons with dark irises. The color of the iris was stated in 97 cases, and in 65 of these the irises were dark and in 32 light, a ratio of 2 to 1. It may also be of some significance that 13 of the cases in the literature

were reported by Italian authors. In addition, 2 of the American reports noted that the patient was Italian. The only other reference to race were to 2 Negro and 2 Jewish patients.

The large number of dark eyes in this series is interesting in view of Goldberg's general study on pigment deposits on the posterior wall of the cornea. His observation was that pigmentation of the cornea was more common with light than with dark irises. On the other hand, Steiner has reported that in the dark Javanese pigmentation of the cornea is seldom encountered. These reports are mentioned because they are at least suggestive that Krukenberg's spindle, observed preponderantly in dark eyes, may not be related to other types of pigmentation of the cornea.

Pigmentary Disturbances in the Eye.—In a considerable number of cases of Krukenberg's spindle there were disturbances of the ocular pigmentation. In 44, nearly one fourth, degeneration of the iris pigment or pigment flecks on the iris were noted. Pigment flecks were present in the anterior chamber in 20, and in 39 the statement was made that no pigment was visible in the anterior chamber. In the remaining cases no mention was made of this factor.

Pigmentation of the lens was noted in 14 cases. In 7 it was in the form of an annular band around the circumference of the lens. These cases all have been reported previously in the literature. The only case of pigmentation of this type in the American literature is that reported by Zentmayer. In 8 cases mention was made of corneal pigmentation in addition to the Krukenberg spindle. In 3 of these there was a pigmented band of the limbus.

Inflammation.—The role of inflammation in the production of Krukenberg's spindle is difficult to evaluate. It seems apparent in some cases that it is a factor of considerable importance, and some authors believe that even when there is no evidence of inflammation some low grade, chronic process must account for degeneration of the ocular pigment. There was a specific history of inflammation of the eye in 25 cases in this series. In 75 cases the statement was made that there was no history of inflammation. In 8 of the former the type of inflammation was not stated. Of the remaining 17 cases, there was choroiditis in 4, iritis in 2, cyclitis in 2, uveitis in 2, iridocyclitis in 1, keratitis in 4, interstitial keratitis in 1 and chorioretinitis in 1.

Trauma.—The number of cases in this series in which there was a history of a foreign body in the cornea or injury to the eye may be of some significance. There were 9 cases of foreign body and 1 of concussion of the eyeball. In another case the patient had worked in front of an electric furnace for a year, and consequently there may have been some trauma to the eyes.

Acquired Diseases of the Eye.—In addition to disturbances of the iris pigment in 44 cases, the presence or history of inflammation of the eye in 25 and pigmentation of the lens in 14 and of the cornea in 8, other ocular conditions, most of them degenerative or senile manifestation, were noted with sufficient frequency to be of some possible significance in relation to Krukenberg's spindle. Cataract was present in 12 cases, glaucoma in 12, detached retina in 10 and vitreous opacities in 10. Corneal opacities were reported in 8 cases, arcus senilis and choroidal atrophy in 4 each, posterior synechias in 2, posterior staphyloma in 2 and optic atrophy in 2. The following conditions were listed in 1 case each: cupped disk, fluid vitreous, conus, uveal cataract and calcareous changes. Some disturbance of the external ocular muscles was present in 4 cases.

General Diseases.—Among the general, or constitutional, diseases noted in the cases of Krukenberg's spindle, none occurred with sufficient frequency to indicate any correlation with the ocular condition. There was tuberculosis in 5, pleurisy in 1 and scrofula in 1. Sinusitis was noted in 2 cases, otitis media in 1, dental pyorrhea in 2 and tonsillitis in 1. Arthritis, myocarditis and hypertension were reported in 1 case each. In 5 cases there was a neurotic state and in 1 asthenia. In 1 there had been a nephrectomy. Diabetes was present in 2 cases, obesity in 1 and endocrine imbalance in 1. There had been an oophorectomy in 1, and in 1 there had been three abortions. There was 1 case of dementia praecox.

Although a few cases have been reported in which there was a history of syphilis, there was only 1 case in this series in which there was a definite history of interstitial keratitis. In another case the patient's brother had had interstitial keratitis but none of the stigmas of congenital syphilis had been discovered in the patient himself. In 19 cases a definite statement was made that the Wassermann reaction was negative, and in 5 it was recorded as positive.

Heredity.—The early observers thought that Krukenberg's spindle represented a congenital defect, yet there is little evidence in the cases to indicate this. The manifestations in mother and daughter have been reported by Strebel and Steiger, Vogt and Seissiger. Mauksch reported the spindle in twin brothers. In a case reported by Sommer, it had been noted in the record of the patient's father that he had corneal pigmentation. Whether this was of the Krukenberg type is not known, since the record was old. In the other case reported by Sommer, however, four children and two grandchildren showed no evidence of pigmentation of the cornea. Seissiger examined forty-one relatives of one of his patients without finding another example of spindle.

In a few other instances some comment was made concerning the condition of the eyes in other members of the patient's family. Kayser, in arguing for the acquired nature of Krukenberg's spindle, pointed out that his patient belonged to a family with megalocornea and yet was the only member who showed pigmentation of the posterior surface of the cornea. In 1 case comment was made that both parents were myopic; in another, that no one else in the family was myopic; in still another, that the patient's brother had myopia also but no spindle.

From these scattered data, there is little to indicate that Krukenberg's spindle is of congenital origin or that there is a hereditary factor in its causation.

Among the congenital defects of the eye mentioned as accompanying the corneal spindle, none could be considered, from the standpoint of incidence, as more than a coincidental finding. In 56 cases it was stated specifically that no congenital defects were present. Two cases each were listed of inverse retinal vessels, embryonal cataract, megalocornea and coloboma of the disk. One case of each of the following defects was noted: congenital lens opacities, vertically oval pupils, coloboma of the iris, ectropion uveas, Mittendorf's dot and inferior conus.

Pupillary Membrane.—Some of the early authors who wrote on Krukenberg's spindle believed that, theoretically at least, this manifestation was related to the presence of a persistent pupillary membrane, and numerous reports appeared of cases of persistent pupillary membrane in which some pigmentation was displayed. In the first decade after Krukenberg's description, the reports contained theoretic discussions and comparisons with "melanosis of the cornea" as described by Krukenberg. These articles have not been included in this review. An excellent discussion of them is to be found in Holloway's article, which appeared in 1910, and also in Edgerton's review.

The attempt to find a relation between persistent pupillary membrane and Krukenberg's spindle was stimulated largely by the belief that the latter was of congenital origin. There is nothing in the present study to indicate that pupillary membrane has anything to do with the appearance of the spindle, because it was present in only 6 cases, with 2 additional instances in which its presence was questionable, while in 66 cases a definite statement was made that there was no evidence of a persistent pupillary membrane. Augstein in 1912 stated definitely that "melanosis of the cornea" has nothing to do with persistent pupillary membrane, and most authors since his time have agreed with him.

COMMENT

In only 2 instances have the eyes of a patient with Krukenberg's spindle been examined pathologically. These were reported by Hanssen and by Kayser. In Hanssen's case a woman who had not been aware

of the presence of a spindle showed extensive degeneration of the retinal layers of the iris pigment and lesser disturbances of the pigment epithelium of the ciliary body. Hanssen expressed the opinion that these represented the obvious origin of the pigment spindle on the posterior surface of the cornea. Kayser's patient was a young man who had first exhibited the pigment spindle about four and one-half years before his death. Pathologic examination showed that the eye was completely healthy except for the pigmentation and entirely normal aside from megalocornea. There were no inflammatory or degenerative changes except extensive disintegration of the retinal layer of pigment in the iris and massive distribution of the epithelial pigment in the anterior section of the bulb, which was absorbed by the endothelial layers of the cornea. Kayser commented that the pathologic changes in his case were entirely similar to those reported by Hanssen. Both of these authors felt that the pathologic evidence pointed to an acquired pathologic condition rather than to a congenital anomaly.

All observers who have written about Krukenberg spindles in recent years are unanimous in the opinion that they represent an acquired condition. Edgerton at the time his report was published still embraced the conception of congenital origin, but in a personal communication he says that he now believes that the spindles are acquired. Certainly the facts elicited in this study of 202 cases tend to confirm the theory that Krukenberg's spindle is an acquired defect. The ocular conditions which were present in a sufficient proportion of cases to suggest that they were more than incidental are myopia, pigmentary disturbances of the iris, inflammatory changes and pathologic changes such as cataract, glaucoma and detached retina. The age of the patients also would indicate an acquired rather than a congenital cause. Eighty per cent of those whose age was reported were more than 30 and 57 per cent were more than 40. Only 20 per cent of the patients were less than 30.

On the other hand, analysis of this series of cases failed to reveal a correlation with any congenital condition, although a variety of congenital defects were noted in 18 cases. There obviously is no correlation between Krukenberg's spindle and persistent pupillary membrane.

Although authorities are agreed that Krukenberg's spindle generally appears in myopic patients, especially women of middle age, the exact mechanism of the formation is not clearly understood. In view of the relatively large number of patients who have some degeneration of the iris or uveal pigment and pigmentation of the cornea, it would appear that some local change in the corneal endothelium or some peculiarity in the circulation of the aqueous, or both, must account for pigmentation which assumes a fusiform arrangement in a vertical line.

Some disintegration of the pigment layers of the iris accounts for the pigment on the posterior surface of the cornea. According to Moeschler, this is true of other types of pigmentation of the cornea as well as of Krukenberg's spindle. Then, through the action of currents of the aqueous in the anterior portion of the eye, there apparently is a tendency, at least in some eyes, for the pigment granules to group themselves in a vertical line. This process has been compared by numerous authors to the Ehrlich-Turk phenomenon. Finally, the pigment is absorbed by the corneal endothelium and becomes deposited in a vertical spindle on the posterior surface of the cornea.

It is impossible to make any positive statement as to how these processes are initiated, but the facts elicited in this study give some basis for speculation. This disintegration of the iris pigment is probably influenced by inflammatory, senile or degenerative changes. Duke-Elder expressed the belief that Krukenberg's spindle is merely the accentuation of a general atrophic process in which pigment derived from the uveal tract is deposited on the corneal endothelium and aggregated into the space of an approximately vertical spindle, although minute examination frequently shows that a much larger area of the cornea is bespeckled to a less degree.

Both Goldberg and Moeschler, who made studies of pigmentation of the cornea, found that the majority of patients in whom it was present were more than 40 years of age and that there was a striking correlation between corneal pigmentation and degeneration of the iris pigment. Whether myopia is an important factor in pigmentary deposits on the cornea other than Krukenberg spindles has not been indicated by the reports in the literature. It would seem more probable that the myopia has an influence on the manner of distribution of pigment, that is in a vertical line, rather than on the pigmentary deposit itself. As Bauer has suggested, this might be through some alteration of the aqueous currents in the elongated myopic eye.

That there is some relation between the typical Krukenberg pigment deposit on the posterior surface of the cornea and epithelial dystrophy has been suggested by Sallmann, Gifford and Kraupa (1920). Goar (1934) reported that in a series of 53 cases of dystrophy of the corneal endothelium, a well marked Krukenberg spindle was present in 4. These cases have not been included in the tabulations, because no details were given and it was not known whether the case of Krukenberg's spindle reported by the same author in 1928 was included in them.

Several other authors (Caramazza, Korobova, Puglisi-Duranti, Kayser, Bauer and Koby) have stated the belief that some local change in the corneal endothelium is necessary to account for the deposition of

the pigment in spindle formation. Senile and other degenerative processes would probably account for this. These might possibly have some endocrine or nutritional factor as a basis.

Although the factor of sex apparently is important in the development of Krukenberg's spindle, with the ratio of females to males 2 to 1, it is difficult to decide just how its influence may be exerted. Since investigators who have studied corneal pigmentation other than Krukenberg's spindle have not noted a similar preponderance of females and since the incidence of myopia is approximately the same in men as in women, it may be that the sex, or endocrine, factor is most important in producing local changes in the cornea which favor the deposition of pigment in a spindle formation. This seems logical in view of Goar's finding that corneal dystrophy was three times as frequent in women as in men.

In postulating an explanation of the formation of Krukenberg's spindle, the only point on which the clinical and pathologic evidence is convincing is that there is disintegration of the iris pigment, probably initiated by inflammatory, senile or degenerative changes. That an additional factor or factors are essential to account for the deposit of pigment on the cornea in spindle form seems logical in view of the large number of cases of corneal pigmentation and pigmentary disturbances of the iris as contrasted with the few cases of Krukenberg's spindle. That the additional factors are exerted in the presence of, or are influenced by, myopia and senile changes, especially anile changes, seems certain in view of the visual difficulties, age and sex of the patients in this series.

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Clinical Notes

PARESIS OF ACCOMMODATION DUE TO DENTAL CARIES

Report of a Case

MORTON E. BROWNELL, M.D., WICHITA, KAN.

In an interesting and enlightening article entitled "Subnormal Accommodation"¹ Dr. Avery De Hart Prangen brought out the close relation between low accommodative power, or paresis of accommodation, and dental diseases. The following case report has been submitted to Dr. Prangen, who agrees with me that it is of unusual interest, particularly as it bears out his assertions.

D. M., a white youth aged 18, first appeared in my office on Sept. 27, 1940. He complained that he could not read at all and was unable to keep up his work in school. The condition had been becoming gradually worse for the past two years. He had no headaches nor any complaint regarding his eyes except that he was unable to read. He had never worn glasses. He was strong and healthy. Physical examination failed to reveal any pathologic condition except a low grade involvement of the antrums and a severe carious condition of all the teeth. The teeth showed a breaking up, or dissolving, of the enamel, and many of them were simply snags. There was some roentgen evidence of periapical infection. The Wassermann reaction was negative.

Examination of the eyes showed a slight tendency at times toward exotropia. The phorometer revealed an exophoria for distance vision which constantly varied from 2 to 10 prism diopters. In accommodation the variation was between 10 and 20 prism diopters and exotropia became apparent. There was no hyperphoria. The adduction varied from nil to 5 prism diopters. The pupils reacted promptly to light both directly and consensually but sluggishly in accommodation and not at all in convergence. The pupils were large but round. The vision in the right eye without correction was 20/20 and in the left eye 20/30. The amplitude of accommodation was 1.2 D. in each eye (Prince rule). An error of 0.25 D. of hyperopic astigmatism was found in the right eye and of 0.25 D. of myopic astigmatism in the left. The refraction was done without cycloplegia because of the low amplitude of accommodation. With correction of the error vision was 20/20 in each eye. It was then found that with the addition of a plus 2.50 D. sph. for the right eye the patient could read 0.62 mm. Jaeger test type at 15 inches (38 cm.). With the left eye addition of a +2.25 D. sph. gave him the same near vision. However, when he attempted to use both eyes it was possible for him to coordinate the images and overcome an apparent diplopia only when a

1. Prangen, A. DeH.: Subnormal Accommodation, Arch. Ophth. 6:906-918 (Dec.) 1931.

2 degree prism base in was placed before each eye, evidence of an associated weakness in convergence.

The fields of vision were entirely normal for form and for color, and the fundi showed no pathologic change.

The patient was given the following prescription for glasses: Right eye: + 0.25 D. cyl. axis 90 \bigcirc + 2.50 D. sph. Left eye: - 0.25 D. cyl. axis 180 \bigcirc + 2.25 D. sph. A 2 degree prism base was ordered incorporated only in the reading segments. The patient was also advised to have all his teeth removed as soon as possible and to return once a month for observation.

He was next seen on November 7, when he returned to report that all his teeth had been removed except the incisors. At that time I found the same degree of exophoria as before, but the range of accommodation without glasses within a half hour showed a variation of from 2.5 to 7.5 D. In other words, the patient was apparently regaining his power of accommodation but fatigue still developed rapidly. I therefore advised him to wear the bifocals only when his eyes felt tired and to do without them as best he could the rest of the time. I also prescribed orthoptic exercises to aid his convergence, which was still very low.

He next appeared at my office on December 12. All his teeth had been removed, and he was wearing plates. He still showed 10 prism diopters of exophoria in accommodation, but his adduction was 16 prism diopters. The vision in each eye without correction was 20/20, and the amplitude of accommodation without glasses was 11.5 D., or normal for his age. He was advised to discard his glasses entirely but to continue with his orthoptic exercises and report back in three months.

At the final examination, on May 12, 1941, he reported that he had been doing close work in an airplane factory from seven and a half to twelve hours a day. When his day's work was completed he was unable to read with comfort, but he was able to carry on all his duties without blurring of the vision. The picture so far as the range of accommodation, muscle balance and vision were concerned was unchanged from that reported in the previous examination.

OPHTHALMOPLAGIC MIGRAINE

Report of a Case

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Ophthalmoplegic migraine was first described in 1890 by Charcot¹ as being closely related to migraine and as including palsy, usually of the third cranial nerve. This ophthalmic disease is relatively infrequent. Among 25,000 medical admissions to the Peter Bent Brigham Hospital, Boston, Stetcher² noted only 1 instance. In a review of the

1. Charcot, J. M., cited by Rea, R. L.: *Neuro-Ophthalmology*, St. Louis, C. V. Mosby Company, 1938.

2. Stetcher, R. N.: *Recurrent Oculomotor Paralysis: Report of a Case*, Boston M. & S. J. **193**:1239-1241 (Dec. 31) 1925.

literature Möbius³ found only 29 cases. Others have been reported by McKay,⁴ Dassen,⁵ Riley⁶ and Elliott.⁷

REPORT OF CASE

History.—R. C., a white woman, married, aged 45, was first seen by an internist in March 1938, at which time a tentative diagnosis of the menopause and hypertension was made. Her blood pressure was 174 systolic and 100 diastolic. Appropriate medical treatment was prescribed.

In September 1939 she complained of a severe migraine headache on the left side of her head, most prominent in the region of the left eye. The attack lasted approximately a week and was followed by some blurring of the vision of the left eye and by diplopia. She stated also that she had been subject to attacks of migraine for the past eight years and that these appeared to be more severe during



Fig. 1.—The patient with ophthalmoplegic migraine of the left eye.

her menstrual period. She had had acute urticaria seventeen years previously and had been told she exhibited allergic manifestations.

In March 1941 she had an acute infection of the upper respiratory tract and was given symptomatic treatment. Two months later she returned with her left

3. Möbius, P. J.: Die Migraine, in Nothnagel, H.: *Specielle Pathologie und Therapie*, Vienna, A. Hölder, 1894, vol. 12, pt. 1, sect. 3.

4. McKay, R. P.: Ophthalmoplegic Migraine, *Am. J. Ophth.* **12**:889-895 (Nov.) 1929.

5. Dassen, R.: Jaqueca oftalmopléjica con parálisis recidivante del III par craneano, *Semana méd.* **1**:1049-1052 (April 16) 1931.

6. Riley, H. A.: Migraine, *Bull. Neurol. Inst. New York* **2**:429-544 (Nov.) 1932.

7. Elliott, A. J.: Ophthalmoplegic Migraine, with Report of a Case, *Canad. M. A. J.* **43**:242-244 (Sept.) 1940.

eye completely closed, as shown in figure 1. One week before she had had what she assumed was an attack of migraine, with severe pain around the left eye. She complained of anorexia, and the smell of food tended to nauseate her. The vision of the left eye began to blur, and diplopia and ptosis developed suddenly.

Examination.—Vision was 20/20 in the right eye and 20/200 in the left. The left pupil was dilated to 8 mm.; the diameter of the right pupil in normal light was 4 mm. There was complete ophthalmoplegia of the left eye, involving both the intrinsic and the extrinsic fibers of the third cranial nerve, as illustrated in figures 2 and 3. Ophthalmoscopic examination revealed moderate narrowing and



Fig. 2.—*A*, dilation of the pupil of the left eye. *B*, paralysis of the left internal rectus muscle.



Fig. 3.—*A*, paralysis of the left inferior rectus muscle. *B*, paralysis of the left superior rectus muscle.

slight sclerosis of the retinal arteries. Both optic disks were normal. A tentative diagnosis of ophthalmoplegic migraine of the left eye was made.

Laboratory Reports.—The blood showed 95 per cent hemoglobin, 4,750,000 red cells and 10,500 white cells. The differential count revealed 70 per cent polymorphonuclear leukocytes, 24 per cent lymphocytes, 5 per cent monocytes and 2 per cent eosinophils. Wassermann and Mantoux tests and urinalysis all gave negative results. Roentgenograms of the skull revealed no evidence of pathologic change.

Treatment and Course.—The patient was given a mild sedative and received diathermy and treatment with an infra-red lamp on alternate days to the region surrounding the left eye. The ptosis disappeared first, the internal ophthalmoplegia next and finally the extraocular palsies. One month after the onset no ocular signs or symptoms were present. The vision in each eye was 20/20. The intra-ocular tension in each eye was 20 mm. (Schiötz), and the visual fields were normal.

A photograph taken four weeks after the onset of the illness is shown in figure 4.

COMMENT

Two hypotheses have been suggested regarding the cause of ophthalmoplegic migraine, namely the hypophysial and the vasomotor theory. According to the former a transitory edema or swelling of the pituitary



Fig. 4.—The patient one month after the onset of the illness.

body takes place. Subsequently pressure on the cavernous sinus and on neighboring nerves produces the characteristic signs and symptoms of migraine and of ophthalmoplegia. This theory was favored by Deyl,⁸ who made a comparative study of the hypophysis cerebri in many cases. He concluded that the unilateral symptoms of migraine may be due to an asymmetry of the pituitary body.

Migraine and its various symptoms have also been explained by the theory of transitory vasomotor changes, or angiospasm. Tzanck⁹ stated the belief that migraine headaches result from spasm of the cranial arteries following excessive autonomic nerve stimulation. In the

8. Deyl, J.: Explication anatomique de la migraine, Cong. internat. de méd., Compt. rend., sec. de neurol., Paris, 1900; cited by Elliott.⁷

9. Tzanck, A.: Le traitement des migraines par le tartrate d'ergotamine. Bull. et mém. Soc. méd. d. hôp. de Paris 52:1057-1061 (June 28) 1928.

experiments of Graham and Wolff¹⁰ a direct relationship was found between the intensity of migraine headaches and the amplitude of pulsations of certain cranial arteries. The administration of ergotamine tartrate decreased the throbbing of these vessels and alleviated the headache. Woltman¹¹ expressed the opinion that the pain of migraine may result from the expansion of relaxed dural arteries brought on by a sudden change in arterial pulsations. According to Wolff¹² the paralysis of ophthalmoplegic migraine may be explained by temporary dilatations or aneurysmal defects of the posterior cerebral artery causing pressure on the oculomotor nerve.

Migraine was found by Lennox¹³ to occur twice as frequently in women as in men, and through the administration of ergotamine tartrate he was able to relieve the headache in 90 per cent of his cases.¹⁴ Burch,¹⁵ commenting on this case, stated: "The association with urticaria makes one feel that migraine may be either an allergic manifestation or a purely angiospastic affair with a toxic causation." Migraine from the allergic viewpoint has been discussed by Sippe.¹⁶

SUMMARY

1. A case of ophthalmoplegic migraine with recovery is reported.
2. The etiology of the condition is discussed.
3. The possibility of allergic manifestations in connection with the disease is mentioned.

10. Graham, J. R., and Wolff, H. G.: Mechanism of Migraine Headache and Action of Ergotamine Tartrate, *Arch. Neurol. & Psychiat.* **39**:737-763 (April) 1938.

11. Woltman, H. W.: The Symptoms of Headache and Some Conditions Suggested by It, *Minnesota Med.* **23**:19-25 (Jan.) 1940.

12. Wolff, H. G., cited by Elliott.⁷

13. Lennox, W. G.; von Storch, T. J. C., and Solomon, P.: The Effect of Ergotamine Tartrate on Non-Migrainous Headaches, *Am. J. M. Sc.* **192**:57-60 (July) 1936.

14. Lennox, W. G.: Migraine and Epilepsy: Newer Concepts and Treatment, *J. Med.* **19**:284-289 (Aug.) 1938.

15. Burch, F. E.: Personal communication to the author.

16. Sippe, C.: Migraine from the Allergic Viewpoint: Results of Treatment in One Hundred and Five Cases, *M. J. Australia* **1**:893-895 (May 21) 1938.

A COMBINATION DILATOR AND IRRIGATION NEEDLE FOR THE LACRIMAL CANAL

BENJAMIN FRIEDMAN, M.D., NEW YORK

The oculist often finds that a punctum which he has dilated preparatory to irrigation of the lacrimal canal has contracted during the moment he turned his back to exchange the dilator for the irrigating syringe.

I have attempted to construct an instrument which will act as a combination dilator and irrigation needle, so that only one step will be involved in the irrigation of the canal. The instrument is in effect a dilator with a central channel, the distal end opening at the tip and the proximal end into an adapter for a standard 2 cc. syringe. The opening is about 0.25 mm. wide, and the tip is about 0.4 mm. over all. The narrow aperture was attained by telescoping a series of fine metal tubes within one another and then smoothing over the joints so as to impart a uniform conical surface to the dilator portion. The instrument is 52 mm. in length and is sturdy enough to withstand the usual handling.¹

For the occasional punctum which requires an exceedingly fine point for dilation the instrument is equipped with a stiff wire stylet. The end of the stylet is drawn out about 0.5 mm. beyond the tip of the needle, and the punctum is then dilated. The stylet is now withdrawn from the proximal end while the needle is held in situ, and the loaded syringe is



connected with the needle. The stylet at other times serves to clean the bore and is kept within the needle while it lies in the instrument cabinet.

1. The instrument was made for me by J. Brandenburg, 122 East Twenty-Fifth Street, New York.

AN INEXPENSIVE SLIT LAMP

JOHN F. DIAS JR., M.D., NEW BEDFORD, MASS.

All ophthalmologists realize the value of the slit lamp, but the cost makes many forego its use. The inexpensive lamp described hereafter has given good service in my office.

THEORY OF THE SLIT LAMP

The slit lamp sold commercially consists essentially of five parts: a concentrated filament lamp, a condenser, a slit, an objective lens and a microscope. The condenser focuses the image of the filament on the objective lens; the objective lens focuses the image of the slit on the cornea, and the microscope furnishes an enlarged image of the cornea. The slit may be any distance from the condenser on the side of the objective lens but is placed close to it, just far enough away so that dust particles on the condenser will be out of focus when the slit is in focus on the cornea (*A* in the accompanying figure).

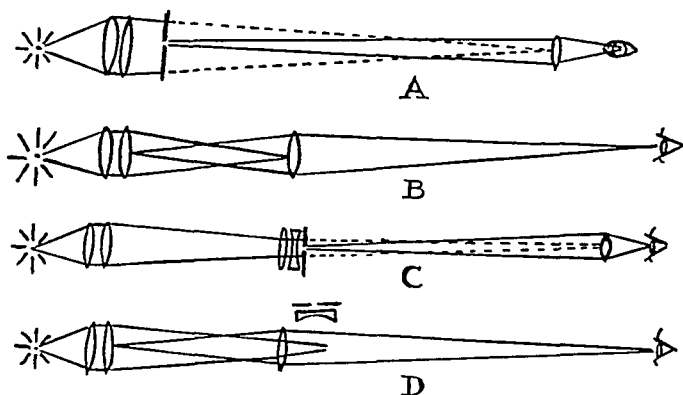
EXAMINATION LAMP

A common type of examining and operating lamp is similar to the slit lamp illuminating system except that the slit is omitted and the

condenser image is focused on the object illuminated, thus furnishing a field of light free from color fringes or dark spots. To give a large field of illumination the objective lens is placed closer to the condenser than it is in the slit lamp, as shown in *B* of the figure. A lamp of this type can be used as a basis for the slit lamp described hereafter, the result being a neat, well finished piece of equipment which does not have a "home-made" appearance.

COMBINATION LAMP

The slit lamp illuminating system which I have devised is based on a combination of the two lamps described (*C* of the accompanying figure). The examining light is a dental lamp in which a 6 volt spot-light bulb is the source of light. The bulb is rotated so that the two legs of the V-shaped filament are in line with the optical axis of the lens system and its distance from the condenser adjusted so that the image of the filament focuses beyond the objective lens just far enough to produce a blurring at the plane of the objective lens that changes the



A, slit lamp illuminating system. *B*, examining light illuminating system. *C*, combination light as slit lamp. *D*, combination light as examining light.

spiral of the filament image into an evenly illuminated band. Since all the light passing through the condenser also passes through the objective lens, the field of illumination produced by the lamp is still free from shadows or color fringes and the use of the lamp as an examining light is unaffected.

A negative spherical lens is inserted in the filter holder of the lamp immediately before the objective lens. This lens is of such strength (-8 D.) that the filament image is brought to focus 2 feet (61 cm.) beyond the objective lens, the distance of the eye in slit lamp work. A stenopaic slit (approximately 0.5 mm. wide) is also inserted in the filter holder, and the lamp is ready for use as a slit lamp. The slit lamp objective lens used is a plus 14 D. lens held in the hand with the little finger and the ring finger braced against the patient's face. In order to obtain a sharper image of the slit, a trial case lens must be fitted with a diaphragm having a 1 cm. hole. A Tillyer or a similar lens would not require the diaphragm. A binocular loupe furnishes the

magnification necessary for an adequate slit lamp examination. This amount of magnification naturally will not show all that a microscope would, but it does show all but the finest details of the cornea, the anterior chamber and the lens, and at a small fraction of the cost.

I have tried using a laboratory microscope with this illuminating system but have not been very successful, because such a microscope has too shallow and too small a field for use with a hand-held lens or without a good support for the chin and the forehead.

For focal illumination, the filter holder, with its lens and slit, is simply swung out of the path of the light and the same hand-held objective is used to concentrate light on the eye.

For general illumination the lamp is used in the usual way, with the lens and slit swung out of the way.

SUMMARY

A slit lamp illuminating system based on a modification of a common type of examining light is described. This system is capable of furnishing a sharply defined narrow beam of light which, with a binocular loupe, may be used for optically sectioning the living eye, for focal illumination and for general illumination.

Ophthalmologic Reviews

EDITED BY DR. FRANCIS HEED ADLER

THEORIES OF CATARACT

JOHN G. BELLOWS, M.D., PH.D.

AND

HERMAN CHINN, PH.D.

CHICAGO

The theories that have been advanced for the pathogenesis of cataract are many and varied. It is beyond the scope of the present review to discuss in detail the vast literature in support or in opposition of each. Instead we shall concern ourselves primarily with the theories that seem to be most amply supported by investigational work—either clinical or experimental. The means by which some types of cataract are produced may often seem far removed from the cause of senile cataract. These factors are included in the discussion, nevertheless, because of the light they may shed on the general problem. The theories may be broadly divided into two groups: (1) those involving physical or chemical derangements and (2) those involving senile involutional and hereditary factors.

The etiologic factors of the former group lend themselves more readily to experimental study and can be conveniently subdivided under the following headings: (1) endocrine dysfunction, (2) decrease in nutrient supply, (3) intoxication of the lens, (4) changes due to radiant energy, (5) alterations in capsular permeability, (6) osmotic changes and (7) refractive errors. These divisions are purely arbitrary. They are by no means mutually exclusive and have been adopted solely to facilitate discussion. A certain amount of repetition is therefore unavoidable.

Much of the support for these theories has been procured by animal experimentation. Caution must be exercised in correlating experimental data with the clinical picture of senile cataract. In the first place, transferring data from one animal to another of a different species is always a hazardous procedure. Secondly, the conditions produced in the laboratory are usually of a more acute nature than those found in human patients. Nevertheless, we believe that this problem can be more profitably investigated by an experimental than by a clinical approach. The

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factors operating in the production of senile cataract may be similar to those produced experimentally, but of a milder nature, so that the formation of lenticular opacities would require longer periods. For example, the cataract produced by experimental pancreatectomy within several months may be analogous to cataract found in an elderly person who has been mildly hyperglycemic for years. Occasionally the clinical symptoms may equal in severity those found in experimental animals, for example in cases of juvenile diabetes or hypoparathyroidism. In such cases cataract develops rapidly.

ENDOCRINE DYSFUNCTION

Clinically, cataract has been observed in association with a variety of endocrine abnormalities—cretinism, mongolian idiocy, tetany, gonadal insufficiency and diabetes. In addition, opacities frequently occur in persons suffering from certain idiopathic conditions which are believed to be dependent on an imbalance of internal secretion, namely myotonic dystrophy, neurodermatitis and scleroderma. Since cataract usually occurs after senile changes of the sex glands, Siegrist¹ postulated that sex hormones are essential in the physiology of the lens. He reported that on the administration of glandular preparations cessation in the progress of cataract occurred and in some cases actual regression could be seen. Such reports are questionable because of the uncertain composition of the preparations and the unconfirmed nature of the work.

The relation between diabetes mellitus and cataract has been repeatedly emphasized in the literature for over a century. In 1798 Saunders² described the onset of bilateral cataract in a diabetic person. Numerous reports of ocular involvement in association with diabetes followed rapidly, so that by the middle of the nineteenth century a considerable literature was available. Leber³ presented an exhaustive review of this early work in his comprehensive article on the subject. Although some investigators⁴ have questioned whether diabetic cataract exists as a distinct clinical entity, the frequency of lenticular opacities in children suffering from diabetes suggests a relation between lenticular changes and diabetes. Further evidences are the transient refractive changes

1. Siegrist, A.: *Der graue Alterstar*, Berlin, Urban & Schwarzenberg, 1928.

2. Saunders, R. H., cited by Rollo, J.: *Cases of the Diabetes Mellitus*, ed. 2, London, J. Callow, 1806.

3. Leber, T.: *Ueber die Erkrankungen des Auges bei Diabetes mellitus*, Arch. f. Ophth. (pt. 3) **21**:206, 1875.

4. Gallus, E.: *Gibt es eine Cataracta diabetica?* Deutsche med. Wchnschr. **45**:658, 1919. Spalding, F. M., and Curtis, W. S.: *Retinitis and Other Changes in the Eyes of Diabetics*, Boston M. & S. J. **197**:165, 1927. Gradle, H. S.: *Diabetes from the Standpoint of the Ophthalmologist*, J. Indiana M. A. **22**:2, 1929. Waite, J. H., and Beetham, W. P.: *The Visual Mechanism in Diabetes Mellitus (A Comparative Study of Two Thousand and Two Diabetics, and Four Hundred and Fifty-Seven Non-Diabetics for Control)*, New England J. Med. **212**:367, 1935.

noted in patients with diabetes and the high frequency of hyperglycemia or lowered dextrose tolerance in patients with cataract.⁵ Proof that diabetes may give rise to cataract is furnished by the experiments of Chaikoff and Lachman.⁶ Of 10 pancreatectomized dogs kept alive by means of insulin for two years, cataract developed in 8. On the other hand, no lenticular opacity appeared in a large number of normal dogs observed during this period. On a careful chemical analysis, Carey and Hunt⁷ found a low phosphorus content to be the only feature differentiating diabetic cataract from the senile type. The significance of this finding is not known. Whether the cataract develops primarily because of insulin insufficiency or as a secondary process is still not settled. Schiötz⁸ and Löwenstein⁹ expressed a belief in the former hypothesis. Most workers, however, believe the ocular changes to result secondarily from abnormal processes initiated by the insulin deficiency.

Schanz¹⁰ has shown that dextrose and acetone appear to sensitize the lens proteins so that they are readily precipitated by light. The importance of this finding may have been overestimated, since other compounds have a similar, and in many cases a more marked, sensitizing action on proteins without playing any known part in the formation of cataract. Kirby and associates¹¹ found acetone and betahydroxybutyric acid to be strongly toxic in vitro to lens epithelium. This toxicity was apparent in the concentrations found in the aqueous humor of diabetic patients. The diabetic acidosis may play a significant role in initiating enzymatic or degradation reactions, since Krause¹² has shown lenticular acidosis

5. O'Brien, C. S.: Hyperglycemia in Persons with Advanced Senile Cataract, *J. A. M. A.* **98**:284 (Jan. 23) 1932. Baldwin, H., and Barthel, E. A. S.: The Relation of Hyperglycemia to Cataract, *ibid.* **83**:994 (Sept. 27) 1924. Langdon, H. M.: The Blood-Chemistry of Patients with Primary Cataract: A Study of the Sugar Tolerance in Aglycosuric Patients with Cataract, *Tr. Ophth. Soc. U. Kingdom* **45**:204, 1925. O'Brien, C. S.: Biochemical Studies of the Blood in Patients with Senile Cataracts, *Tr. Am. Ophth. Soc.* **26**:438, 1928.

6. Chaikoff, L., and Lachman, G. S.: Occurrence of Cataract in Experimental Pancreatic Disease, *Proc. Soc. Exper. Biol. & Med.* **31**:237, 1933.

7. Carey, H., and Hunt, H. M.: The Chemical Nature of Cataract in the Diabetic, *New England J. Med.* **212**:463, 1935.

8. Schiötz, C.: *Norsk mag. f. lægevidensk.* **74**:1201, 1913; cited by Duke-Elder, W. S.: *Text-Book of Ophthalmology*, St. Louis, C. V. Mosby Company, 1940, vol. 3, p. 3209.

9. Löwenstein, A.: Ueber die klinische und histologische Form der innersekretorischen Katarakt. Versuch einer Abgrenzung, *Arch. f. Ophth.* **132**:224, 1934.

10. Schanz, F.: Die Wirkung des Lichtes auf die lebenden Organismen, *Biochem. Ztschr.* **71**:406, 1915.

11. Kirby, D. B.; Estey, K. C., and Wiener, R. von E.: Effect of Changes in Medium on Cultures of Lens Epithelium, *Arch. Ophth.* **10**:37 (July) 1933.

12. Krause, A. C.: The Chemistry of the Lens: IV. The Nature of the Lenticular Proteins, *Am. J. Ophth.* **17**:507, 1934.

to stimulate the action of beta protease, an enzyme attacking the lens protein. Changes in capsular permeability,¹³ degeneration of the ciliary epithelium¹⁴ and osmotic upsets¹⁵ have also been postulated as explanations for the diabetic cataract. The last-mentioned theory seems to account best for the accumulated observations. Dextrose and salt disturbances among the blood, aqueous humor and lens set up an abnormal interchange of water which causes first refractive changes and later opacities. This will be discussed more thoroughly in a later section.

Hypoparathyroidism cataract is not uncommon. It results most frequently from surgical injury or excision of the parathyroid glands during thyroidectomy. Parathyroprival tetany was first produced experimentally by Erdheim,¹⁶ in 1906. By administering calcium to parathyroidectomized dogs Luckhardt and Blumenstock¹⁷ and Dragstedt and associates¹⁸ kept them alive long enough for cataract to form. The time required for lenticular opacities to appear varied with the size of the animal. Thus, Goldmann¹⁹ detected subcapsular changes in rats within a few hours after tetanic convulsions. In larger animals, including man, opacities may not appear for many months or years after removal of or injury to parathyroid glands (in the dog within two years²⁰; in man within twenty years²¹).

The parathyroid glands apparently function by maintaining a normal blood calcium level and thus indirectly a normal ionic balance. Most interest has been centered about the tetanic convulsions in the etiologic study of hypoparathyroidism cataract. Originally it was thought that the opacity developed as a result of the nutritional disturbance following

13. Bellows, J., and Rosner, L.: Biochemistry of the Lens: XI. Effect of Galactose on Permeability of the Capsule of the Lens, *Arch. Ophth.* **20**:80 (July) 1938.

14. Peters, A.: Ueber die Entstehung des Schichtstaars und verwandter Staarformen, *Arch. f. Ophth.* (pt. 1) **39**:221, 1893.

15. Duke-Elder, W. S.: (a) Changes in Refraction in Diabetes Mellitus, *Brit. J. Ophth.* **9**:167, 1925; (b) The Pathological Action of Light upon the Eye, *Lancet* **1**:1137, 1168 and 1250, 1926.

16. Erdheim, J.: Tetania parathyreopriva, *Mitt. a. d. Grenzgeb. d. Med. u. Chir.* **16**:632, 1906; cited by Goldmann.¹⁹

17. Luckhardt, A. B., and Blumenstock, J.: Additional Observations on Completely Thyroparathyroidectomized Dogs, *Am. J. Physiol.* **63**:409, 1923.

18. Dragstedt, L. R.; Sudan, A. C., and Phillips, K.: Studies on the Pathogenesis of Tetany: IV. The Tetany of Oestrus, Pregnancy and Lactation, *Am. J. Physiol.* **69**:477, 1924.

19. Goldmann, H.: Experimentelle Tetaniekatarakt, *Arch. f. Ophth.* **122**:146, 1929.

20. Edmunds, W.: Double Cataract Following Experimental Total Thyroidectomy in a Dog, *Proc. Roy. Soc. Med. (Sect. Ophth.)* **9**:56, 1916.

21. Heine, L.: Ueber Tetanie und Myotoniekatarakt, *Ztschr. f. Augenh.* **55**:1, 1925.

a spasm of the ciliary muscle during tetany.²² In support of this theory it was claimed that the cataract following electric or lightning shock, ergotism or eclampsia was due to the associated convulsions.^{22b} The failure of the ciliary spasm due to wormwood oil or strychnine poisoning to cause cataract casts serious doubt on this theory.²³ Furthermore, experimental work on electric cataract indicates that this opacity might be more adequately explained by other variations.²⁴

Weinstein²⁵ expressed the belief that tetanic cataract has a toxic basis and attributed the lenticular changes to an accumulation of tyramine, histamine and guanidine, which reduces the stability of the lens. The relation of variations in the blood calcium level to the development of cataract is poorly understood. Adams²⁶ and Eisman and Luckhart²³ could not produce cataract by feeding calcium lactate to rabbits, although the calcium content of the plasma and the aqueous was increased. Nor were these investigators able to obtain opacities by lowering the amount of calcium in the blood stream. Von Bahr suggested that a lowered calcium content of the aqueous humor during tetany increases the capsular permeability and makes the lens more susceptible to injury by some unidentified colloid. This theory will be considered in more detail when the toxic action of various substances is discussed. In harmony with this, Clark^{26a} on the basis of in vitro studies concluded that the absence of parathyroid hormone increases the permeability of the lens capsule. Another explanation is based on Cameron's²⁷ theory that tetany depends on a disturbance in equilibrium between the concentrations of calcium and hydroxyl ions on the one hand and of sodium, potassium and hydrogen on the other. If there is a sufficient decrease of one of the ions of the first group or an increase of any in the second group tetany occurs. Similarly, an upset in the ionic composition of the lens may lead to changes in its colloidal structure.

The cause of myotonia dystrophica is unknown but seems likely to be endocrinal. Although only 300 cases have been reported in the

22. (a) Peters, A.: Weiteres über Tetanie und Staarbildung, *Ztschr. f. Augenh.* **5**:89, 1901. (b) Wettendorfer, F.: Ein Beitrag zur Aetiologie des juvenilen Totalstaars, *Wien. med. Wchnschr.* **47**:528, 1897.

23. Eisman, C., and Luckhardt, A. B.: Mechanism of Cataract Formation in Thyroparathyroidectomized Dogs, *Proc. Soc. Exper. Biol. & Med.* **25**:6, 1927.

24. Bellows, J., and Chinn, H.: Biochemistry of the Lens: XIV. Pathogenesis of Electric Cataract, *Arch. Ophth.* **26**:606 (Oct.) 1941.

25. Weinstein, P.: Parathyroid Cataract, *Brit. J. Ophth.* **17**:236, 1933.

26. Adams, D. R.: The Role of Calcium in Senile Cataract, *Biochem. J.* **23**:902, 1929.

26a. Clark, J. H.: Effect of Parathyroid Hormone on Permeability of Lens Capsule to Calcium, *Am. J. Physiol.* **126**:136, 1939.

27. Cameron, A. T.: *Recent Advances in Endocrinology*, Philadelphia, P. Blakiston's Son & Co., 1934.

literature, Allen and Barer²⁸ expressed the opinion that the condition is not as rare as is ordinarily assumed. They reported 22 cases themselves, observed over a period of eight years, in which every patient displayed lenticular changes. Greenfield²⁹ first pointed out that the lenticular opacities found in patients with this disease are an important part of the syndrome. The condition is hereditary, with the cataract appearing at progressively earlier ages in each successive generation. The direct etiologic agent for the cataract is not known. Krause³⁰ stated the belief that the lenticular changes are related to a disturbed creatine metabolism. Just how this would operate is not clear. Terrien and co-workers³¹ claimed that the cataract results from a "premature senescence."

Cataract develops in a high percentage of mongolian idiots.³² It has also been noted in persons with cretinism,³³ neurodermatitis (atopy),³⁴ scleroderma,³⁵ poikiloderma atrophicans vasculare³⁶ and chronic eczema.³⁷ Differentiation among the various dermatogenic conditions is difficult. The cause is unknown, but the conditions are thought in many cases to result from some endocrine dysfunction or

28. Allen, J. H., and Barer, C. G.: Cataract of Dystrophia Myotonica, Arch. Ophth. **24**:867 (Nov.) 1940.

29. Greenfield, J. G.: Notes on a Family of "Myotonia Atrophica" and Early Cataract, with a Report of an Additional Case of "Myotonia Atrophica," Rev. Neurol. & Psychiat. **9**:169, 1911.

30. Krause, A. C.: Chemical Pathogenesis of Cataract, Am. J. Ophth. **21**:1343, 1938.

31. Terrien, F.; Sainton, P., and Veil, P.: Cataracte héréditaire, familiale, et myopathie, Arch. d'ophth. **46**:193, 1929.

32. Pearce, F. H.; Rankin, R., and Ormond, A. W.: Notes on Twenty-Eight Cases of Mongolian Imbeciles, with Special Reference to Their Ocular Condition, Brit. M. J. **2**:186, 1910. Weil, G., and Nordmann, J.: La cataracte et ses rapports avec la pathologie générale, Ann. d'ocul. **163**:401, 1926.

33. Goulden, C.: Some Unusual Forms of Acquired Cataract, Tr. Ophth. Soc. U. Kingdom **48**:97, 1928. Jeremy: Cataracts in a Mongolian Idiot, Proc. Roy. Soc. Med. (Sect. Dis. Child.) **14**:11, 1921.

34. (a) Rothmund, A.: Ueber Cataracte in Verbindung mit einer eigenthümlichen Hautdegeneration, Arch. f. Ophth. (pt. 1) **14**:158, 1868. (b) Beetham, W. P.: Atopic Cataracts, Arch. Ophth. **24**:21 (July) 1940.

35. Werner, C. W. O.: Ueber Katarakt in Verbindung mit Sklerodermie, Inaug. Dissert., Kiel, Schmidt & Klaunig, 1904; cited by Beetham.^{34b} Vossius, A.: Zwei Fälle von Katarakt in Verbindung mit Sklerodermie, Ztschr. f. Augenh. **63**:640, 1920.

36. Schnyder, W. F.: Ueber Katarakt im Kindesalter bei gleichzeitigem Vorkommen von Poikiloderma atrophicans. Familiäres Vorkommen in der Schweiz (Rothmund'sche Krankheit), Schweiz. med. Wchnschr. **65**:719, 1935. Rothmund.^{34a}

37. Vogt, A.: Weiteres Ergebnisse der Spaltlampenmikroskopie des vordern Bulbusabschnittes, Arch. f. Ophth. **109**:154, 1922.

imbalance. That cataract and cutaneous disorders should be related seems not improbable when one recalls the ectodermal origin of the lens.

Buschke and co-workers³⁸ attributed the cataract developing in rats fed thallium salts to endocrine disorders. Extensive changes were observed in the testicles and in the adrenal glands of these poisoned animals.

Not only may deficiencies of the various hormones result in cataract, but with at least one hormone an excess may produce similar changes. Schultz³⁹ described the toxic effect of epinephrine on the mouse. It was found that cataract rapidly appeared after the injection of epinephrine and then underwent complete reversal. The onset was facilitated by administration of histamine.⁴⁰ With rats it was necessary to superimpose the injection of epinephrine on a moderate degree of histamine shock before the opacities developed. Tum Suden⁴¹ attributed the opacity to a disturbance of carbohydrate metabolism with a concomitant circulatory embarrassment.

DECREASE IN NUTRIENT SUPPLY

The transparency of the lens depends on the proper utilization of nutrient material supplied by the aqueous humor. If for any reason there is a local deficiency of some vital constituent, the lens becomes opaque. This condition may be produced in a number of ways—surgically, clinically or experimentally. Ligation of the posterior ciliary arteries⁴² or the vortex veins⁴³ resulted in cataract. The deposition of dyes on the capsule, impeding the normal interchange of foodstuffs and

38. Buschke, A.: Demonstration von Mausekatarakten nach Verfütterung von Thallium, *Ztschr. f. Augenh.* **48**:302, 1922. Buschke, A.; Löwenstein, L., and Joel, W.: Weitere histologische Befunde bei experimenteller chronischer Thalliumvergiftung, *Klin. Wchnschr.* **7**:1515, 1928. Ginsberg, S., and Buschke, A.: Ueber die Augenveränderungen bei Ratten nach Thalliumfütterung (Katarakt und Iritis) und ihre Beziehungen zum endokrinen System, *Klin. Monatsbl. f. Augenh.* **71**:385, 1923.

39. Schultz, W. H.: Quantitative Pharmacological Studies: Adrenalin and Adrenalin-Like Bodies, *Hygienic Laboratory Bulletin* 55, United States Treasury Department, Public Health Service, 1909; cited by Tum Suden.⁴⁰

40. Tum Suden, C.: Opacities of the Lens Induced by Adrenaline in the Mouse, *Am. J. Physiol.* **130**:543, 1940.

41. Tum Suden, C., and Wyman, L. C.: Adrenaline Induced Opacities of the Lens in the Rat, *Endocrinology* **27**:628, 1940.

42. Wagenmann, A.: Experimentelle Untersuchungen über den Einfluss der Circulation in den Netzhaut- und Aderhautgefassen auf die Ernährung des Auges, insbesondere der Retina, und über die Folgen der Sehnervendurchschneidung, *Arch. f. Ophth.* (pt. 4) **36**:1, 1890.

43. Koster Gzyn, W.: Beiträge zur Lehre vom Glaukom, *Arch. f. Ophth.* (pt. 2) **41**:30, 1895. von Geuns, J. R.: Ueber Entstehung von Cataract nach Unterbindung der Venae vorticosae, *ibid.* **47**:249, 1898.

waste products, also terminated in opacities.⁴⁴ Clinically, uveal vascular stasis or congestive glaucoma may have similar reactions.

The cataract of ergot poisoning has been laid to defective nutrition of the lens resulting from an arterial spasm.⁴⁵ It was believed that the epithelial lining of the ciliary body and the posterior surface of the iris are changed by this action. In like manner, many workers⁴⁶ expressed the belief that disturbed nutrition can account for the cataract produced with naphthalene. This theory was postulated on the basis of impaired ciliary function. The ciliary involvement, however, is variable and seems hardly severe enough to produce the observed changes.⁴⁷

Severe inanition⁴⁸ and acute thirst⁴⁹ also resulted in visual disturbances due partly to lenticular opacities. The cataract that has been reported in association with numerous severe infective diseases—for example diphtheria, cholera, scarlet fever and typhus—may have been due partially to the cachetic state of the patient. A tryptophan deficiency causes cataract to form in rats.⁵⁰ In salamanders, deprivation of cystine and to a lesser extent of glycine and glutamic acid seemed to have similar results.⁵¹ Generalized avitaminosis has been cited by many workers as an important cause of cataract.⁵² Early work of von Szily

44. Friedenwald, J. S.: Permeability of the Lens Capsule, with Special Reference to the Etiology of Senile Cataract, *Arch. Ophth.* **3**:182 (Feb.) 1930.

45. Orloff, K.: Changes in the Eyes in Chronic Poisoning by Ergot and Its Derivatives, *Nevrol. vestnik* (no. 1) **12**:100, 1904; abstracted, *Arch. f. Augenh.* **53**:9, 1905.

46. Hess, C.: Der Naphthalinstar, in *Pathologie und Therapie des Linsensystems*, in Graefe, A., and Saemisch, E. T.: *Handbuch der gesamten Augenheilkunde*, ed. 3, Leipzig, Wilhelm Engelmann, 1911, vol. 6, pt. 2, chap. 9, p. 225. Sala, P.: Ueber Veränderungen an den Ciliarepithelien bei Naphthalinvergiftung, *Klin. Monatsbl. f. Augenh.* **41**:1, 1903.

47. Saffner, O.: Zur pathogenese des Naphthalinstars, *Arch. f. Ophth.* **59**:520, 1904.

48. Farina: *Lettura oftal.* **4**:529, 1927; cited by von Szily.¹⁰⁷

49. Kudo, T.: Studies on the Effects of Thirst: I. Effects of Thirst on the Weights of the Various Organs and Systems of Adult Albino Rats, *Am. J. Anat.* **28**:399, 1921.

50. Curtis, P. B.; Hauge, S. M., and Kraybill, H. R.: The Nutritive Value of Certain Animal Protein Concentrates, *J. Nutrition* **5**:503, 1932. Totter, J. R., and Day, P. L.: Cataract and Other Ocular Changes Resulting from Tryptophane Deficiency, *J. Biol. Chem.* **140**:cxxxiv, 1941.

51. Patch, E. M.: Cataract as a Result of Dietary Deficiency in Larval *Amblystoma Tigrinum*, *Science* **79**:57, 1934; Cataracts in *Amblystoma Tigrinum* Larvae Fed Experimental Diets, *Proc. Soc. Exper. Biol. & Med.* **46**:205, 1941; Dietary Production of Cataracts in Larval *Amblystoma Tigrinum*, *J. Nutrition* **22**:365, 1941.

52. (a) Yoshimoto, R.: Beitrag zur Frage der Avitaminosen des Auges, *Arch. f. Augenh.* **99**:160, 1928. (b) von Szily, A., and Eckstein, A.: Neuer Beitrag zur

and Eckstein^{52b} indicated that cataract might result from vitamin A deficiency. This has been disproved repeatedly. The effects observed by the early workers were probably secondary to other ocular involvements.^{52c} Cataract may follow vitamin D deficiency. The changes observed are similar to those described as occurring with parathyroid insufficiency. Rachitic animals do not acquire tetany unless sufficient phosphates in alkaline form are added to the diet so that the level of calcium drops while that of phosphorus rises. Tetany appears when the blood calcium level drops below 7 mg. per hundred cubic centimeters, and shortly after this lenticular opacities appear.⁵³

The primary cause of the cataract is universally believed to be the tetanic condition rather than the uncomplicated rickets. Von Bahr⁵³ reviewed the evidence in favor of this concept. Convincing support has recently been added by Bietti,⁵⁴ who produced cataract in rats fed a low calcium diet. These rats presented typical "rachitic tetanic" cataract although no roentgenologic evidence of rickets could be found. Rauh,^{54a} however, although confirming the production of cataract on a calcium-poor diet, found rickets present invariably.

Inseparably bound up with the nutrition of the lens is the auto-oxidative system found therein. The fact that three fundamental oxidation-reduction systems, those of glutathione, ascorbic acid and possibly riboflavin, are markedly decreased during the onset of cataract of widely diverse types seems highly significant. Derangement of such systems deprives the lens fibers of normal respiratory potentialities, and their death becomes inevitable. With death the fibers lose their transparency and opacities appear. The question arises as to how such a derangement develops. One possibility lies in a nutritional deficiency of an essential constituent. Fischer⁵⁵ has claimed repeatedly that the riboflavin content of the cataractous lens is decreased. On the contrary, other workers

Frage der experimentellen Starerzeugung bei jungen Ratten durch Vitaminmangel der Nahrung, *Klin. Wchnschr.* **4**:919, 1925. (c) Jess, A.: Ueber kongenitale und vererbare Starformen der weissen Ratte, nebst Bemerkungen über die Frage des Verhaltens der Linsen bei vitaminfreier Ernährung, *Klin. Monatsbl. f. Augenh.* **74**:49, 1925.

53. von Bahr, G.: Studies on the Aetiology and Pathogenesis of Cataracta Zonularis, *Acta ophth.*, 1936, supp. 11.

54. Bietti, G.: Ueber eine rein tetanische Ernährungskatarakt, *Klin. Monatsbl. f. Augenh.* **105**:299, 1940.

54a. Rauh, W.: Ueber rachitische Knochenveränderungen bei der angeblich "rein tetanischen" Ernährungskatarakt, *Klin. Monatsbl. f. Augenh.* **107**:59, 1941.

55. Fischer, F. P.: Die fluorescierenden Substanzen der Linse, *Arch. f. Augenh.* **108**:544, 1933; Der Flavinegehalt der Linse, *Arch. f. Augenh.* **109**:468, 1936; Linse und Glaskörper, *Ophthalmologica* **96**:167, 1938; Ueber die gelbbraunen Farbstoffe der Linse, *ibid.* **99**:425, 1940.

have been unable to detect riboflavin in significant quantities even in normal lenses.^{55a} It has been demonstrated that a deficiency of this substance produces cataractous changes. This was shown first by Day, Langston and O'Brien,⁵⁶ in 1931, and rapidly confirmed.⁵⁷ The minuteness of the quantity of riboflavin necessary to prevent the opacity probably accounts for the low incidence of the production of cataract observed by some authors⁵⁸ in rats fed diets supposedly free from riboflavin. Although an absolute deficiency of riboflavin in man seems unlikely, clinicians are demonstrating that a relative deficiency is surprisingly widespread.⁵⁹ Conceivably a decreased intake of riboflavin may be a contributing factor in the pathogenesis of some cataractous states. However, in view of the inability of some workers to demonstrate riboflavin in the normal lens and of the pathologic change in other ocular

55a. Rochat, G. F.: Ist das Laktoflavin in einer einzigen menschlichen Linse nachweisbar?, *Klin. Monatsbl. f. Augenh.* **103**:432, 1939. von Euler, H., and Günther, G.: Zur Kenntnis der Diaphorase-Vorkommens in Blut und in Augenlinsen, *Ztschr. f. physiol. Chem.* **256**:229, 1938. von Euler, H.; Hellström, H.; Schlenk, F., and Günther, G.: Die Enzymsysteme des oxydo-reduktiven Stoffwechsels in Augenlinsen, *Arch. f. Ophth.* **140**:116, 1939. von Euler, H., and Adler, E.: Ueber das Vorkommen von Flavinen in tierischen Geweben, *Ztschr. f. physiol. Chem.* **223**:105, 1934. György, P.: Investigations on the Vitamin B₂ Complex: II. The Distribution of Lactoflavin and of the "Pellagra-Preventive Factor" (Vitamin B₆) in Natural Products of Animal Origin, *Biochem. J.* **29**:760, 1935.

56. Day, P. L.; Langston, W. C., and O'Brien, C. S.: Cataract and Other Ocular Changes in Vitamin G Deficiency: Experimental Study on Albino Rats, *Am. J. Ophth.* **14**:1005, 1931.

57. O'Brien, C. S.: Experimental Cataract in Vitamin G Deficiency, *Arch. Ophth.* **8**:880 (Dec.) 1932. Morgan, A. F., and Cook, B. B.: Cataract Producing and Dermatitis Producing Nutritional Factors, *Proc. Soc. Exper. Biol. & Med.* **34**:281, 1936. Day, P. L.; Darby, W. J., and Langston, W. C.: The Identity of Flavin with the Cataract Preventive Factor, *J. Nutrition* **13**:389, 1937. Day, P. L.; Darby, W. J., and Cosgrove, K. W.: The Arrest of Nutritional Cataract by the Use of Riboflavin, *ibid.* **15**:83, 1938. El-Sadr, M. M.: Eye Lesions Associated with Riboflavin Deficiency in Rats, *Chemistry & Industry* **58**:1020, 1939.

58. Eckardt, R. E., and Johnson, L. V.: Nutritional Cataract and Relation of Galactose to Appearance of Senile Suture Lines in Rats, *Arch. Ophth.* **21**:315 (Feb.) 1939. Bourne, M. C., and Pyke, M. A.: Occurrence of Cataract in Rats Fed on Diets Deficient in Vitamin B₂, *Biochem. J.* **29**:1865, 1935.

59. Sydenstricker, V. P.; Geeslin, L. E.; Templeton, C. M., and Weaver, J. W.: Riboflavin Deficiency in Human Subjects, *J. A. M. A.* **113**:1697 (Nov. 4) 1939. Jolliffe, N.; Fein, H. D., and Rosenblum, L. A.: Riboflavin Deficiency in Man, *New England J. Med.* **221**:921, 1939. Kruse, H. D.; Sydenstricker, V. P.; Sebrell, W. H., and Cleckley, H. M.: Ocular Manifestations of Ariboflavinosis, *Pub. Health Rep.* **55**:157, 1940. Sydenstricker, V. P.; Sebrell, W. H.; Cleckley, H. M., and Kruse, H. D.: Ocular Manifestations of Ariboflavinosis: A Progress Note, *J. A. M. A.* **114**:2437 (June 22) 1940.

structures in riboflavin deficiency, the concomitant lenticular changes may be only secondary in nature.

It has been demonstrated repeatedly that a decrease of glutathione in the lens precedes the onset of galactose cataract and that this diminution is one of the earliest indications of lenticular alteration.⁶⁰ In this connection, the detoxifying action of cysteine on naphthalene must be remembered. Bourne and Young⁶¹ have established that in the rabbit naphthalene is excreted in the urine as a mercapturic acid derivative, which is a conjugation product of naphthalene and cysteine. As a result of the detoxifying process, the animal suffers a reduction in the endogenous cysteine proportional to the amount of the drug administered. All tissues, including the lens, show a diminution of their sulfhydryl-containing compounds, largely glutathione. One of the important functions of glutathione is the protection of ascorbic acid against oxidation. It would be expected, therefore, that the vitamin C content would also be affected in cataract. The concentration in an opaque lens has been shown to be markedly diminished.⁶² It has also been reported that a subnormal content of the vitamin is present in the blood and in the urine of elderly cataractous persons and that this deficiency may create a predisposition toward the formation of cataract.⁶³ However, these findings have been questioned by Karbacher,⁶⁴ who found no significant decrease in the tissue saturation of vitamin C in cataractous persons. Furthermore, scurvy is rarely accompanied by cataract.

INTOXICATION OF THE LENS

Many attempts have been made, with a fair degree of success, to explain cataract on a basis of the production of toxin. Certainly there

60. Bellows, J.: *Biochemistry of Lens: IX. Influence of Vitamin C and Sulfhydryls on the Production of Galactose Cataract*, *Arch. Ophth.* **16**:762 (Nov.) 1936.

61. Bourne, M. C., and Young, L.: *The Metabolism of Naphthalene in Rabbits*, *Biochem. J.* **28**:803, 1934.

62. van Euler, H., and Martius, C.: *Ueber den Gehalt der Augenlinsen an Sulfhydrylverbindungen und an Ascorbinsäure*, *Ztschr. f. Physiol. Chem.* **222**:65, 1933. Fischer, F. P.: *Die reduzierenden Substanzen der Linse*, *Arch. f. Augenh.* **108**:527, 1933. Nordmann, J., and van Wien, H.: *Déterminations précises de la teneur en vitamin C du cristallin normal et cataracté*, *Bull. Soc. d'ophth. de Paris* **46**:136, 1934. Bellows, J.: *Biochemistry of the Lens: VII. Some Studies on Vitamin C and the Lens*, *Arch. Ophth.* **16**:58 (July) 1936.

63. Bellows, J.: *Biochemistry of the Lens: V. Cevitamic Acid Content of the Blood and Urine of Subjects with Senile Cataract*, *Arch. Ophth.* **15**:78 (Jan.) 1936. Seefried, J.: *Ueber den Vitamin C- Haushalt der Altersstarkranken*, *Arch. f. Ophth.* **138**:620, 1938.

64. Karbacher, P.: *Kritische Bemerkungen zu Johannes Seefrieds Arbeit: "Ueber den Vitamin C- Haushalt der Altersstarkranken," Arch. f. Ophth.* **140**:748, 1939.

appears to be a large group of lenticular opacities whose direct relation to toxins of various types cannot be disavowed. Unfortunately, there are varieties of cataract which can be included in this group only by a callous disregard of experimental evidence. Infective foci have been frequently blamed as an etiologic factor,⁶⁵ but no experimental work has ever unequivocally demonstrated such a relation. Certain general systemic poisons, however, rapidly produce opacities, for example thallium,³⁸ ergot,⁶⁶ dinitrophenol,⁶⁷ dinitro-orthocresol,⁶⁸ naphthalene⁶⁹ and paradichlorobenzene.⁷⁰

In the present state of knowledge it is uncertain whether these substances produce cataract because of cytoplasmic poisoning or because of a derangement in the metabolism of the lens. Their toxic effects on the eye vary with the species. Thus, thallium³⁸ produces cataract in the rat but not in man, whereas dinitrophenol causes cataract in man⁶⁷ but not in laboratory animals. Naphthalene if ingested gives rise to cataract in man⁷¹ and in the rabbit.⁶⁹ When phthalic acid, which damages the kidney, is injected before naphthalene is fed, cataract occurs more rapidly and uniformly.⁴⁷ This type of cataract has been the one most commonly produced experimentally, because it closely resembles the subcapsular

65. Romer, P.: Untersuchungen über das biologische Verhalten des Blutserums zum Linseneiweiss bei Katarakt: I. Mitteilung. Der gegenwertige Stand der Lehre von der Entstehung des subcapsularen Altersstaars, *Arch. f. Augenh.* **76**:120, 1914.

66. Taube, J.: Die Geschichte der Kriebel-Krankheit, besonders derjenigen welche in den Jahren 1770 und 1771 in den Zellischen Gegenden gewüthet hat, Göttingen, J. C. Dieterich, 1872; cited by Barger, G.: Ergot and Ergotism, London, Gurnen & Jackson, 1931, p. 31. Meier, I.: Ueber die Entwicklung des grauen Staars in Folge der Kriebelkrankheit (Raphania), *Arch. f. Ophth.* (pt. 2) **8**:120, 1861.

67. Boardman, W. W.: Rapidly Developing Cataract After Dinitrophenol, *J. A. M. A.* **105**:108 (July 13) 1935. Horner, W. D.; Jones, R. B., and Boardman, W. W.: Cataracts Following the Use of Dinitrophenol: Preliminary Report of Three Cases, *ibid.* **105**:108 (July 13) 1935. Lindberg, J. G.: Eight Cases of Dinitrophenol Cataract, Two of Them with Punctated, Stationary Opalescences of the Lens of a Type Not Hitherto Described, *Acta ophth.* **16**:556, 1938.

68. Mahlen, A.: Zur Kenntniss der Katarakta bei Dinitroorthokresolbehandlung, *Acta ophth.* **16**:563, 1938; Tabelle über Augenuntersuchungen an mit Dinitroorthokresol behandelten Patienten, *ibid.* **17**:215, 1939.

69. Bouchard and Charrin: La cataracta par la naphtaline, *Compt. rend. Soc. de biol.* **38**:614, 1886. Adams, D. R.: The Nature of the Ocular Lesions Produced Experimentally by Naphthalene, *Brit. J. Ophth.* **14**:49, 1930; A Study of the Correlation Between the Biochemical and Intraocular Changes Induced in Rabbits by the Administration of Naphthalene, *ibid.* **14**:545, 1930.

70. Berliner, M. L.: Cataract Following the Inhalation of Paradichlorobenzene Vapor, *Arch. Ophth.* **22**:1023 (Dec.) 1939.

71. Lezenius A.: Ein Fall von Naphthalinkatarakt beim Menschen, *Klin. Monatsbl. f. Augenh.* **40** (pt. 1):129, 1902; Bemerkung zum Artikel des Herrn Dr. J. v. d. Hoeve "Chorioretinitis beim Menschen durch die Einwirkung von Naphthalin," *Arch. f. Augenh.* **57**:115, 1909.

senile variety in man. An interesting observation was the hyperglycemic state produced by naphthalene in the rabbit.⁷² Simultaneous administration of insulin with the naphthalene retarded the onset of cataract. The opacities resulting during the feeding of naphthalene may therefore be related to diabetic cataract.

The cataract resulting from the feeding of galactose or lactose⁷³ has also been explained on a toxic basis. Mitchell⁷⁴ expressed the belief that it is a result of injury to the epithelium of the lens by the sugar. Her opinion was based on the much earlier observation of Kirby and his collaborators¹¹ that a low concentration of a solution of galactose (as compared with that of a solution of dextrose) is toxic to tissue cultures of lens epithelium. Darby and Day⁷⁵ demonstrated the cataractogenic action of xylose, postulating that in action it is similar to galactose because of their stereochemical similarity. It is possible that in addition to the direct toxic action of galactose on the lens fibers there is an indirect action. If the galactose was detoxified by a compound essential for lenticular metabolism, the depletion of this substance might result in cataract. This would be due primarily to impaired nutrition of the lens but secondarily to the toxin (galactose). The possibility that such a condition occurs with naphthalene poisoning has already been discussed. With galactose cataract there resulted a loss of lenticular glutathione similar to that produced by the feeding of naphthalene.⁶⁰ Furthermore, it was demonstrated that this loss occurred before the onset of the lenticular opacities. However, it is difficult to maintain the analogy between naphthalene cataract and galactose cataract. In the first place, no galactose-cysteine conjugation product has as yet been isolated from the urine of galactose-fed rats. Secondly, although galactose may be harmful to the lens epithelium, it is not a systemic toxin when taken in moderate amounts, as lactose, which contains it, is the chief source of carbohydrates for the young mammal. In fact, the presence of cerebrosides in the body suggests that galactose is essential to the normal development of nerve tissue. Yudkin and Arnold⁷³ stated the belief that the toxic action of galactose is related to calcium

72. Michail, D., and Vancea, P.: Sur la multiplicité des voies par lesquelles on peut produire des lésions oculaires naphthaliniques, *Compt. rend. Soc. de biol.* **96**: 63, 1927; L'action de l'insuline sur l'évolution de la cataracte naphthalinique, *ibid.* **96**:65, 1927; La courbe de la glycémie au cours de l'intoxication naphthalinique, *ibid.* **96**:1456, 1927.

73. Mitchell, H. S., and Dodge, W. M.: Cataracts in Rats Fed on High Lactose Rations, *J. Nutrition* **9**:37, 1935. Yudkin, A. M., and Arnold, C. H.: Cataracts Produced in Albino Rats on a Ration Containing a High Proportion of Lactose or Galactose, *Arch. Ophth.* **14**:960 (Dec.) 1935.

74. Mitchell, H. S.: Cataract in Rats Fed on Galactose, *Proc. Soc. Exper. Biol. & Med.* **32**:971, 1935.

75. Darby, W. J., and Day, P. L.: Xylose as a Cataractogenic Agent, *Proc. Soc. Exper. Biol. & Med.* **41**:507, 1939.

metabolism. This is in harmony with the findings of Mitchell,⁷⁴ who reported the calcium content of cataractous lenses from galactose-fed rats to be three or four times that of lenses from control rats. The findings that the calcium in the lens remained unchanged during the formation of cataract⁷⁶ and that additional calcium entered only after the cataract was mature make it difficult to accept any such explanation.

Recently von Bahr⁷⁷ suggested that the tetanic cataract occurring in calcium deficiency and rickets also belongs in the category of the toxic cataract. His theory is an intriguing one and is supported by in vitro experiments on explanted lenses kept alive by Bakker's⁷⁸ technic. Von Bahr claimed that the lowered calcium content of the aqueous humor resulting from the hypocalcemia causes an increase in the permeability of the lens capsule. This in turn allows the penetration of an unknown colloidal agent which is toxic to the lens fibers. Normally this compound is present in greatest concentration in the red blood cells. Presumably traces of the colloid diffuse into the plasma and thence into the aqueous humor. The sequence of events described for the hypocalcemic animal beautifully demonstrates the interrelation among various theories discussed in this review and the futility of explaining the accumulated data by any all-inclusive theory.

Since the liver is one of the most important detoxifying organs of the body, a relation between hepatic damage and cataract from toxic agents is possible. No direct experimental work is available in support of this statement, but a limited amount of presumptive evidence can be marshaled in its defense. Berliner⁷⁹ has recently reported cataract to result from the inhalation of paradichlorobenzene fumes. Clinical and experimental evidence was submitted to show that hepatic damage was an invariable accompaniment. Onfray and Gilbert-Dreyfus⁷⁹ postulated a similar hepatic damage in dinitrophenol poisoning. Such relations, however, are still in the speculative stage. The hyperglycemia resulting from naphthalene feeding and the marked hepatic degeneration in the diabetic person are other indications pointing in this direction. We have been uniformly unsuccessful in producing cataract in rats after damaging the liver by various means.⁸⁰

76. Bellows, J., and Rosner, L.: Unpublished data.

77. von Bahr, G.: The Influence of Calcium Deficiency on the Surviving Rabbit's Lens (An Experimental Study on the Pathogenesis of Cataracta Tetanica). *Acta ophth.* **18**:170, 1940.

78. Bakker, A.: Eine Methode, die Linsen erwachsener Kaninchen ausserhalb des Körpers am Leben zu erhalten, *Arch. f. Ophth.* **135**:581, 1936.

79. Onfray and Gilbert-Dreyfus: *Bull. Soc. franç. d'ophth.* **1**:114, 1937; cited by Duke-Elder, W. S.: *Text-Book of Ophthalmology*, St. Louis, C. V. Mosby Company, 1940, vol. 3.

80. Bellows, J., and Chinn, H.: Unpublished data.

CHANGES DUE TO RADIANT ENERGY

The fundamental cause of cataract in many of its forms according to Duke-Elder^{15b} is the action of radiant energy directly on the lens itself. Radiant energy, whether manifesting itself as light, heat, roentgen rays, radium or electrical effects, is believed to be composed of electromagnetic vibrations. All radiations transmit energy to the substances which absorb them. The longer waves cause a heating effect, while the short waves produce photochemical and photoelectrical effects. The end result would therefore be essentially the same with all types of radiant energy. The radiation might either affect the lens directly, causing an opacity, or produce changes in the ciliary body, so that the lens would lose its transparency secondarily to alteration in the nutrient fluid. The cataract resulting from the latter cause would thus actually be due to a nutritional deficiency.

Obviously, only the portion of the radiant energy not absorbed by the cornea can influence the lens. The cornea absorbs heat waves longer than 20,000 angstrom units. The shorter waves are partly absorbed and partly transmitted. Transmission is almost complete from the beginning of visible red rays (7,500 angstrom units) down to the ultraviolet region (3,500 units). Below this wavelength the absorption by the cornea again becomes considerable. The lens has two means of protecting itself from the rays which reach it: first, by dispersion and deflection of the rays, and, secondly, through a transformation of the short visible waves into long visible ones which are less active and more easily transmitted.

The influence of ultraviolet rays in the pathogenesis of cataract is thought by some investigators to be considerable. As evidence the high incidence of cataract in India⁸¹ or in the Arctic region⁸² is set forth. In these two sections the ultraviolet content of the sunlight is especially high. Also, farmers and other rural workers have a higher incidence of cataract than persons not exposed to as intense sunlight.⁸³ Further support for this theory is the customary site of incipient cataract in the lower nasal quadrant. This is the area that receives most of the rays. However, the same observation has been quoted in support of the idea that senile cataract may result from refractive errors. The proponents of this theory state that accommodative efforts cause the greatest stress on the zonules attached to the lower nasal quadrant. Excessive traction

81. Hirschberg, J.: Ueber den Star der Glasblaser, *Centralbl. f. prakt. Augenh.* **22**:113, 1898. Snell, S.: An Inquiry into the Alleged Frequency of Cataract in Bottle Makers, *Brit. M. J.* **1**:8, 1907.

82. Daland, J.: Eskimo Snowblindness and Goggles, *Ophth. Rec.* **26**:116, 1917.

83. Salit, P. W.: Sex Incidence of Cataract with Especial Reference to Its Exogenous Causes, *Acta ophth.* **18**:309, 1940.

here may result in incipient lenticular damage, eventually causing cataract. The ultraviolet light presumably initiates a photochemical reaction which alters the lens proteins, enabling more drastic alterations to supervene slowly. It has been shown that irradiation insufficient to produce coagulation induces chemical and physical changes in the lens proteins, making them more labile and more coagulable by various agents.⁸⁴ Furthermore, Adams⁸⁵ and Shoji⁸⁶ reported a decreased glutathione content of lenses exposed to ultraviolet rays. This loss would decrease the metabolic efficiency of the lens. Duke-Elder^{15b} stated that radiation causes an increase of the permeability of the capsule. This might lead to a loss of glutathione and a change in the concentration of the salts and fluids sufficient to bring about opacities in a lens made more vulnerable by short waves. In agreement with this, we found that exposure to ultraviolet light causes an increased swelling of the lens when it is immersed in a hypotonic solution.⁸⁷ It should be remembered, however, that swelling is not necessarily an indication of the state of capsular permeability. Parsons⁸⁸ expressed the opinion that no definite lenticular opacity follows long exposure to ultraviolet and to visible rays. Similarly, Rohrschneider⁸⁹ reported that the irradiation must be so severe as to produce a corneal burn before an opacity develops. The exact status of ultraviolet irradiation in the development of cataract remains unsettled.

An extremely interesting finding in this connection is that of Howell,⁹⁰ who noted that animals sensitized with hematoporphyrin and exposed to sunlight showed lenticular opacities. This photosensitization is strongly suggestive of pellagra, in which severe dermatitis may be precipitated by exposure to sunlight. In pellagrins the excretion of porphyrin is markedly increased and is thought to be a sensitizing agent for the cutaneous eruption.⁹¹ Since the skin and lens are embryologically

84. Burge, W. E.: The Mode of Action of Ultra-Violet Radiation in Injuring Living Cells with Special Reference to Those Constituting the Eye, *Am. J. Physiol.* **39**:335, 1916.

85. Adams, D. R.: Investigations of the Crystalline Lens, *Proc. Roy. Soc., London*, s.B **98**:244, 1925.

86. Shoji, Y.: Sur la cystéine du cristallin et ses rapports avec les rayons ultra-violets, *Arch. d'ophth.* **48**:28, 1931.

87. Bellows, J., and Chinn, H.: Biochemistry of the Lens: XV. Studies on the Swelling of the Isolated Lens, *Am. J. Ophth.* **24**:979, 1941.

88. Parsons, J. H.: Some Effects of Bright Light on the Eyes, *J. A. M. A.* **55**:2027 (Dec. 10) 1910.

89. Rohrschneider, W.: Linsenschädigung durch ultraviolette Strahlen im Tierversuch, *Arch. f. Ophth.* **135**:282, 1936.

90. Howell, cited by Clark, J. H.: Lighting in Relation to Public Health, Baltimore, Williams & Wilkins Company, 1924, p. 163.

91. Spies, T. D.; Gross, E. S., and Sasaki, Y.: Effect of Yeast and Nicotinic Acid in Porphyrinuria, *Proc. Soc. Exper. Biol. & Med.* **38**:128, 1938. Spies, T. D.; Sasaki, Y., and Gross, E. S.: A Note on the Relationship of Porphyrinuria to Human Pellagra, *South. M. J.* **31**:483, 1938.

similar, it would be interesting to investigate the relation between pellagra and cataract. The high incidence of cataract in India, where both intense sunlight and deficient diets are prevalent, suggests further such a relation. A statistical analysis of the cataract incidence among pellagrins should clarify this question.

According to Kraupa,⁹² as early as 1739 the surgeon Heister⁹³ noted cataract in human beings following exposure to fire. The relation between heat and cataract was extended by de Wenzel (1788)⁹⁴ and Beer (1817).⁹⁵ The incidence of this cataract among glass makers was reported by Meyhofer in 1886.⁹⁶ Since then reports have been numerous, with Vogt⁹⁷ and Goldmann⁹⁸ and their respective schools among the most active investigators. Schanz and Stockhausen⁹⁹ stated the belief that the opacity in glassblower's cataract results from the ultraviolet rays emitted from the molten glass. The majority of investigators, however, disagree with this conclusion. Crookes¹⁰⁰ found that ultraviolet rays from molten glass are absorbed by the cornea. However, the infra-red rays from this source were very powerful, and he concluded that the lesion is due to the heat rays. Vogt⁹⁷ divided infra-red waves into two divisions: (1) long waves—15,000 to 20,000 angstrom units—which are nonpenetrating and are absorbed by the corneal surface and (2) short waves 15,000 to 7,500 units—which are capable of penetrating the

92. Kraupa, E.: *Der Glasblaserstar*, Arch. f. Augenh. (supp.) **98**:85, 1928.

93. Heister, L. D.: *De oculorum suffusione sive cataracta*: VIII. *Cataractae causa quae sit*, in *Institutiones chirurgicae, opus triginta annorum*, Amsterdam, J. Waesberg, 1739, vol. 2, sect. 2, chap. 55, p. 598.

94. de Wenzel, J.: *Abhandlungen vom Star*, Uebersetzung der französischen Ausgabe vom Jahre 1786, Nuremberg, 1788; cited by von Szily.¹⁰⁷

95. Beer, G. J.: *Lehre von den Augenkrankheiten*, Vienna, Camesina, Huebner u. Valke, 1817, vol. 2; cited by von Szily.¹⁰⁷

96. Meyhofer: *Zur Aetiologie des grauen Stars*. Jugendliche Katarakte bei Glasmachern, Klin. Monatsbl. f. Augenh. **24**:49, 1886.

97. Vogt, A.: *Einige Messungen der Diathermansie des menschlichen Augapfels und seiner Medien, sowie des menschlichen Oberlides, nebst Bemerkungen zur biologischen Wirkung des Ultrarot*, Arch. f. Ophth. **83**:99, 1912; *Der Feuerstar*, Klin. Monatsbl. f. Augenh. **91**:721, 1933.

98. Goldmann, H.: *Kritische und experimentelle Untersuchungen über den sogenannten Ultrarotstar der Kaninchen und den Feuerstar*, Arch. f. Ophth. **125**:313, 1930; *Experimentelle Untersuchungen über die Genese des Feuerstars*: I. Mitteilung, *ibid.* **128**:413, 1932; II. *Ueber Arbeitshyperthermie bei Feuerarbeitern*, *ibid.* **128**:648, 1932; III. *Die Physik des Feuerstars*. I. Teil, *ibid.* **130**:93, 1933; IV. *Die Physik des Feuerstars*. II. Teil, *ibid.* **130**:131, 1933; V. *Die Physik des Feuerstars*. III. Teil, *ibid.* **130**:140, 1933.

99. Schanz, F., and Stockhausen, K.: *Zur Aetiologie des Glasmacherstars*, Arch. f. Ophth. **73**:563, 1909.

100. Crookes, W.: *The Preparation of Eye-Preserving Glass for Spectacles*, Phil. Tr. Roy. Soc., London, s.A **214**:1, 1914.

cornea. Parsons⁸⁸ described the change in the lens due to infra-red rays as a well defined disk of opacity in the center of the posterior part of the cortex.

Investigators disagree as to the manner in which heat waves exert their injurious effects on the lens. Vogt and his followers expressed the belief that heat waves have a direct influence on the lens; that is, they are specifically absorbed and cause colloidochemical changes in the lens. On the other hand, Goldmann and others insisted that heat waves injure the lens indirectly, the iris being the mediating agent. Proof for the latter theory depends largely on the observation that cataract develops much more rapidly in pigmented animals than in albino animals. Bakker¹⁰¹ presented similar findings arrived at with explanted lenses. He demonstrated that lenses exposed to infra-red radiation do not develop opacities unless covered by iris tissue. Wagner, a student of Vogt, vigorously disputed the conclusions of Goldmann and Bakker, since albino rabbits as well as pigmented ones had cataract after infra-red irradiation.^{101a}

The first reports of lenticular opacities following exposure to roentgen rays were by Chalupecky¹⁰² in 1897 and Guttman¹⁰³ and Treutler¹⁰⁴ in 1905. During the next few years numerous cases¹⁰⁵ were observed in which the cataract developed after the therapeutic use of roentgen rays for various ocular conditions. Opacities developed slowly after the irradiation, taking weeks and even months to reach maturity. Radium treatment produced similar effects. Meesmann¹⁰⁶ reported a case in which the cataract developed nine years after exposure.

The theories for the action of roentgen rays and of radium are poorly documented. Although the lens fibers are thought to be attacked directly,

101. Bakker, A.: Ueber die Bedeutung der Regenbogenhaut für die Entstehung des Infrarots, *Arch. f. Ophth.* **139**:677, 1938; Vergleichende Untersuchungen über das Verhalten der Linse und der Hornhaut gegenüber infraroten Strahlen, *ibid.* **141**:180, 1939.

101a. Wagner, H.: Pathologische und therapeutische Wirkungen des penetrierenden Ultrarot auf das Auge, *Arch. f. Ophth.* **138**:486, 1938; Bemerkungen zu Angriffen Bakkers in der Ultrarotsfrage, *ibid.* **140**:190, 1940.

102. Chalupecky: Ueber die Wirkung der Röntgenstrahlen, *Centralbl. f. Augenh.* **21**:386, 1897.

103. Guttman: Starbildung durch Röntgenstrahlung, *Ber. ü. d. Versamml. d. ophth. Gesellsch.* (1905) **32**:337, 1906.

104. Treutler: Starbildung durch Röntgenstrahlen, *Ber. u. d. Versamml. d. ophth. Gesellsch.* (1905) **32**:338, 1906.

105. Paton: A Case of Posterior Cataract Commencing Subsequent to Prolonged Exposure to X-Rays, *Tr. Ophth. Soc. U. Kingdom* **29**:37, 1909. Axenfield, T.: Doppelseitiges Glioma retinae und intraokulare Strahlentherapie, *Klin. Monatsbl. f. Augenh.* **54**:61, 1915.

106. Meesmann, A.: Beitrag zur Röntgen- Radiumstrahlenschädigung der menschlichen Linse, *Klin. Monatsbl. f. Augenh.* **81**:259, 1928.

the possibility exists that the primary action is on the ciliary epithelium, which in turn modifies the normal transparency of the lens.¹⁰⁷

The cataract following lightning or electric shock differs from that due to roentgen rays or to radium in the speed of its onset. Hess¹⁰⁸ in 1888 reported that changes in the lens epithelium were apparent microscopically within fifteen to thirty minutes after an animal was shocked with a high voltage current. The macroscopic changes after lightning shock had already been described by St. Yves,¹⁰⁹ in 1722, and those after electric shock, by Desbrières and Bargo, in 1905.¹¹⁰ The two opacities were shown to be similar if not identical. The theories explaining the pathogenesis of electric cataract are numerous. These include actual coagulation of the protein,¹¹¹ tears of the lens capsule,¹¹² sustained contraction of the ciliary muscle,¹¹³ disease of the nerve fibers,¹¹⁴ changes due to the action of the ultraviolet rays produced by the electricity¹¹⁵ and many others. The explanations receiving widest support were those by Vossius¹¹⁶ and by Hess. The former stated the belief that the iridocyclitis present was the etiologic factor. Von Szily,¹⁰⁷ Kiribuchi¹¹⁷ and Frese¹¹⁸ agreed with this concept. Hess pointed out the marked

107. von Szily, A.: Linse, in Henke, F., and Lubarsch, O.: *Handbuch der speziellen pathologischen Anatomie und Histologie*, Berlin, Julius Springer, 1937, vol. 11, pt. 3.

108. Hess, C.: *Pathologie und Therapie des Linsensystems*, in Graefe, A., and Saemisch, E. T.: *Handbuch der gesamten Augenheilkunde*, ed. 3, Leipzig, Wilhelm Engelmann, vol. 6, pt. 2, chap. 9, p. 237.

109. de St. Yves, C.: *Les causes accidentelles, qui peuvent blesser la vue, in Nouveau, traite des maladies des yeux, 1722, Paris, P. A. Le Mercier, p. 368; cited by von Szily.*¹⁰⁷

110. Desbrières and Bargo: *Un cas de cataracte due à une décharge électrique industrielle*, *Ann. d'ocul.* **133**:118, 1905.

111. Leber, T.: *Ueber Katarakt und sonstige Augenaffectationen durch Blitzschlag*, *Arch. f. Ophth.* **28**:255, 1882.

112. Yvert, L. A.: *Traité pratique et clinique des blessures du globe de l'oeil*, Paris, Germer, Baillièrre & Cie, 1880, p. 211; cited by von Szily.¹⁰⁷

113. Knies, M.: *Ein Fall von Augenaffectation durch Blitzschlag*, *Arch. f. Ophth.* **32**:236, 1886.

114. Silex, P.: *Beitrag zur Kasuistik der Affektionen infolge von Blitzschlag*, *Arch. f. Augenh.* **18**:65, 1887.

115. Widmark, J.: *The Effect of Strong Light on the Crystalline Lens*, *Hygiea* **63**:641, 1901; abstracted, *Ztschr. f. Augenh.* **7**:173, 1902. Silfvast, J.: *A Case of Ocular Lesions Due to Lightning*, *Finska läk.-sällsk. handl.* **44**:273, 1902; abstracted, *Ztschr. f. Augenh.* **9**:320, 1903.

116. Vossius, A.: *Ein Fall von Blitzaffektion der Augen*, *Beitr. z. Augenh.*, 1892, no. 4, p. 1; cited by von Szily.¹⁰⁷

117. Kiribuchi, K.: *Experimentelle Untersuchungen über Katarakt und sonstige Augenaffectationen durch Blitzschlag*, *Arch. f. Ophth.* **50**:1, 1900.

118. Frese, H.: *Ueber das Spaltlampenbild der Cataracta electrica mit experimentellen Untersuchungen an Kaninchen*, *Arch. f. Augenh.* **91**:278, 1922.

epithelial changes following the shock. He and his supporters maintained that necrosis of the capsular epithelium initiates alterations of the lens terminating in cataract. On the basis of *in vitro* studies of lenses exposed to high voltage currents, we believe that changes in the permeability of the individual fibrillar capsules may also play an important role.²¹

CAPSULAR ALTERATIONS

It is obvious that any abnormality in the capsular membrane might lead to changes in the lens fibers, since the avascular lens must depend on its immediate surroundings for its supply of nutrients. Substances in the aqueous humor when entering the lens must pass through the capsule of the lens, and waste products from the lens must penetrate the capsule in the opposite direction.

Some investigators have considered abnormalities in capsular permeability as important factors in the production of cataract. Hess¹⁰⁸ showed that the normal capsule is fully permeable to water and to electrolytes. Friedenwald,¹¹⁹ in experiments on isolated capsules, demonstrated that they act as semipermeable membranes and that the ease with which substances pass through the capsule varies inversely with the size of the molecule. Gifford and his co-workers,¹²⁰ in experiments on the capsule *in situ*, confirmed Friedenwald's observations and showed further that the permeability of the capsule of a cataractous lens is approximately the same as that of a normal lens. They also found that albumin and glutathione diffuse through the capsule of the lens with difficulty, whereas globulin does not pass through until postmortem changes have affected the capsule. Borley and Tainter¹²¹ obtained negative results when attempting to explain dinitrophenol cataract on the basis of altered capsular permeability.

As has already been discussed, the glutathione content rapidly diminishes when galactose is fed. The opinion was originally entertained that the glutathione might have diffused from the lens because of an increase in capsular permeability resulting from the action of the galactose. Bellows and Rosner¹³ showed, however, that the lens capsule undergoes a decrease in permeability when placed in a galactose solution. The results obtained with dextrose were similar but less marked. It appears possible that galactose and dextrose have a synergistic action, although insufficient data are available to prove this point.

119. Friedenwald, J. S.: The Permeability of the Lens Capsule to Water, Dextrose and Other Sugars, *Arch. Ophth.* 4:350 (Sept.) 1930; footnote 44.

120. Gifford, S. R.; Lebensohn, J. E., and Puntenney, I. S.: The Biochemistry of the Lens: I. The Permeability of the Capsule of the Lens, *Arch. Ophth.* 8:414 (Oct.) 1932.

121. Borley, W. E., and Tainter, M. L.: Effects of Dinitrophenol on the Permeability of the Capsule of the Lens, *Arch. Ophth.* 18:908 (Dec.) 1937.

Further support of the effect of galactose in diminishing the permeability of the capsule of the lens is suggested by the work of Sasaki.¹²² He has shown that the lenses of rats fed dextrose contain a high amount of reducing sugar while those of rats fed galactose possess only normal amounts, in spite of the fact that the aqueous humor of rats fed galactose contains much greater amounts of reducing sugar than that of rats fed dextrose.

Changes in the capsular permeability are intimately associated with the state of nutrition of the lens. A decreased permeability would offer a barrier to the normal interchange of nutrients and waste materials, which in turn could cause lenticular changes due either to deficiency of vital constituents or to an excess of a toxic compound. The reduction of glutathione in the cataractous lens is illustrative of this mechanism. Such an explanation would account for the cataract resulting so frequently from iridocyclitis. The deposition of cells, pigment, protein and other exudative material on the lens capsule would markedly diminish the permeability, with subsequent impairment of nutrition. The cataract resulting from heterochromia or secondarily from endophthalmitis in general might be explained on the same basis. Furthermore, the cataract following the presence of a foreign body in the eye (iron and copper) might in some cases be due to the colloidal deposition of the metal. This would be analogous to the cataract produced by Friedenwald by precipitating nontoxic dyes on the lens capsule.⁴⁴

OSMOTIC CHANGES

In the passage of nutrient material from the blood to the lens two barriers must be traversed, namely the ciliary processes (blood-aqueous) and the lens capsule (aqueous-lens). The same two barriers in reverse order oppose the removal of the waste products of lenticular metabolism. Concentration gradients exist across each of these barriers, gradients that change continually. Thus, there is operative at all times a dynamic equilibrium of osmotic forces between the lens and the aqueous on the one hand and between the aqueous and the blood on the other. Not only is there a continuous interchange of food and waste products, but there is a simultaneous and delicately balanced alteration of the water content. Normally these alterations do not interfere with vision, but in pathologic states the balance may be upset to such a degree that refractive changes and finally death of the lens result.

122. Sasaki, T.: Untersuchungen der Linse, des Blutes und des Kammerwassers von Ratten bei Galaktoseverfütterung: II. Mitteilung. Ueber die Linsenkapselpermeabilität und über den Zuckergehalt von Blut, Kammerwasser, und Linse bei der Galaktosekatarakt, *Arch. f. Ophth.* **138**:365, 1938.

Lenses dropped into hypertonic solutions became opaque¹²³ but regained their transparency when replaced in isotonic solutions. Similarly, cataract has been produced in vivo by administration of a hypertonic solution subcutaneously,^{123a,c} orally,^{123a} rectally,^{123a} subconjunctivally,¹²⁴ intraocularly,¹²⁵ intraperitoneally,^{123c} intralenticularly¹²⁶ and intravenously.⁴⁷ Erlanger¹²⁷ obtained similar results by introducing sodium chloride and barium salts into the eye iontophoretically.

We¹²⁸ have recently shown that the cataract resulting from these agents is due primarily to the osmotic effect of the hypertonic solution. After intravenous administration a wide variety of electrolytes and non-electrolytes proved effective cataractogenic agents. In this group were sodium chloride, sodium sulfate, lithium chloride, ethyl alcohol, sodium lactate, glycerin, ethylene glycol, aminoacetic acid, galactose and a phosphate buffer. The chemical individuality of these compounds suggests that the active mechanism is nonspecific, most likely osmotic. Although our experiments indicate strongly that the production of cataract by the injection of a hypertonic solution is due mainly to an osmotic derangement, certain observations point to other contributory factors. Thus, different substances in solutions of the same tonicity showed wide variations in the degree and in the time of the formation of cataract. Furthermore, the slit lamp and ophthalmoscopic picture was not identical with all compounds.

In a diabetic person the abnormal concentration of dextrose in the blood and in the aqueous humor simulates that obtained by the injection of a hypertonic solution. The hyperglycemia is complicated by the lowered sodium chloride content of the serum. As has already been mentioned, cataract is not uncommon in young patients with the severe form of diabetes. In the early hyperglycemic stages the eye becomes

123. (a) Kunde, F.: Ueber Wasserentziehung und Bildung vorübergehender Katarakte, *Ztschr. f. Wissensch. Zool.* **8**:466, 1857; cited by Deutschmann. (b) Deutschmann, R.: Untersuchungen zur Pathogenese der Katarakt, *Arch. f. Ophth.* **23**:127, 1877. (c) Richardson: Report Before the Medical Society of London, *M. Times & Gaz.* **1**:319, 1860.

124. Manca, G., and Ovio, G.: Studio intorno alla cataratta artificiale, *Arch. di ottal.* **6**:69, 1898; cited by von Szily.¹⁰⁷

125. Panico, E.: Cataratta da cloruro de sodio, *Ann. di ottal. e clin. ocul.* **57**:613 1929; cited by von Szily.¹⁰⁷ Collevati, cited by von Szily.¹⁰⁷

126. Selenkowski, J.: Zur Frage der experimentellen Stare im Zusammenhang der künstlichen Reifungunreifer oder unvollständiger Stare, *Russk. oftal.* **3**:613, 1925; cited by von Szily.¹⁰⁷

127. Erlanger, G.: Katarakterzeugung durch Iontophorese: Experimentelle Studien, *Klin. Wchnschr.* **7**:2391, 1928.

128. Bellows, J., and Chinn, H.: Biochemistry of the Lens: XIII. Production of Lens Opacities by Injection of Hypertonic Solutions, *Arch. Ophth.* **25**:796 (May) 1941.

myopic, while later droplets of fluid are deposited beneath the capsule, with opacities eventually resulting. Although the water exchange seems the most important alteration, other contributing factors due to the abnormal concentration of dextrose in the eye may enter into the picture. The sensitizing action of dextrose and of acetone on the lens protein has already been mentioned. High concentrations of dextrose have also been shown to decrease the permeability of the lens capsule.¹²⁹ Such a decrease would accentuate the osmotic differences across the membrane and might also interfere with the metabolism by decreasing the elimination of waste products or the availability of essential nutrients.

The cataract produced by the feeding of galactose and of xylose appears entirely analogous to the diabetic type with one important exception. These sugars are not utilized as readily by the body as dextrose. Therefore, hyperglycemia results far more easily than with dextrose.¹²⁹ The increased sugar content of the blood produces a similar condition in the aqueous humor, and the profound osmotic disturbance between the aqueous humor and the lens results in an eventual alteration of the lens itself. Bellows and Rosner¹³⁰ and Sasaki¹²² have shown that galactose may appear in the aqueous in relatively high concentrations. Darby and Day⁷⁵ suggested that the chemical similarity between xylose and galactose may somehow account for their cataractogenic properties. Such an assumption is now unnecessary. It is likely that any compound not readily utilized by the body and reaching a high concentration in the blood and in the aqueous humor would similarly produce cataract if administered in adequate quantities. In support of this contention is the observation that arabinose, whose molecule is geometrically distinct from that of galactose and that of xylose, produced cataract when injected intravenously. The effects of galactose on the capsular permeability might increase its effectiveness as a cataractogenic agent. Whether xylose and arabinose similarly alter the lens capsule has never been investigated.

Cataract frequently develops in patients with cholera. This disease is characterized by violent and extensive diarrhea, which produces profound dehydration. A marked osmotic and fluid disturbance of the lens would seem unavoidable in patients with cholera. Dehydration through deprivation of water alone, with resulting cataract, has been described.⁴⁹ In association with tetanic cataract of both the rachitic and the hypopara-

129. Day, P. L.: Blood Sugar in Rats Rendered Cataractous by Dietary Procedures, *J. Nutrition* **12**:395, 1936. Darby, W. J., and Day, P. L.: Blood Sugar Levels in Rats Receiving the Cataractous Sugars Galactose and Xylose, *J. Biol. Chem.* **133**:503, 1940.

130. Bellows, J., and Rosner, L.: Studies on Galactose Cataract, *Am. J. Ophth.* **20**:1109, 1937.

thyroid type a marked ionic imbalance is present and appears to be fundamentally concerned in the production of the opacities.

At present there is insufficient evidence on which to base a discussion of the theory of the remaining types of cataract as related to salt changes and osmotic upsets. We believe, however, that later work will extend the applicability of this theory. For example, naphthalene, dichlorobenzene and possibly other cataractogenic poisons are thought to cause hepatic damage. Since such damage sets up a sequence of metabolic disturbances, cataract might result from the consequent deranged water metabolism or osmotic relations in the lens. Furthermore, naphthalene is known to produce hyperglycemia. The hyperglycemia probably changes the permeability of the capsule, causing an alteration in the concentration of the salts and of the fluids. Cataract formed by radiant energy is thought by Duke-Elder to have a similar pathogenesis, occurring after the lens proteins have been made more vulnerable by the various rays. Thallium causes extensive renal and adrenal damage, which would further upset the normal osmotic balance of the blood and tissue fluids. Until further data are available, however, there is little value in such largely speculative considerations.

REFRACTIVE ERRORS

The purely physical causes of cataract have been stressed by Schoen,¹³¹ Jackson¹³² and others. These workers have attributed the opacities to increased efforts of accommodation resulting in tears in the capsule due to the excessive traction of the zonular fibers. Hypermetropia and astigmatism according to Burdon-Cooper¹³³ have a much greater influence on the production of lenticular opacities than myopia because of the increased or unequal accommodative effort. One difficulty in accepting this theory is the relaxed condition of the zonule during accommodation (Helmholtz). The failure of cataract to develop after prolonged ciliary spasms is another serious objection to this theory. Thus, extensive use of miotics or convulsions in strychnine or oil of wormwood poisoning²³ produced no cataractous changes despite sustained spasms of the ciliary muscle.

131. Schoen, W.: Ueberanstrengung der Accommodation und deren Folgezustände, Beitrag zur Etiologie des Glaucoms und der Aequatorialcataract, Arch. f. Augenh. **17**:1, 1887; Die Ursache des grauen Stars, *ibid.* **19**:77, 1889.

132. Jackson, E.: Causes of Senile Cataract, Am. J. Ophth. **21**:264, 1938.

133. Burdon-Cooper, J.: The Doyne Memorial Lecture: The Etiology of Cataract, Brit. J. Ophth. **6**:385 and 433, 1922.

HEREDITARY FACTORS

Vogt¹³⁴ stated the belief that senile cataract can be explained largely on a hereditary basis. He maintained that the tendency toward early or late degeneration of the lens fibers is inherited. The fundamental lenticular change is genetically induced according to his contention. Cataract becomes then nothing more than a senile involutional change, with the time of its appearance governed by hereditary factors. It may be compared with the graying of hair, which develops at widely differing ages, depending on the individual person. Further evidence in support of the hereditary origin is the observation by Vogt that in uniovular twins cataractous changes identical in type and location occur in the two even when environmental conditions differ greatly. In addition, ophthalmologists have long known that certain types of cataract (pyramidal, punctate, coronary, nuclear and cortical) are often familial and may be transmissible. Without discounting the importance of these findings, it is apparent that hereditary factors cannot explain completely the diverse findings in cases of senile cataract.

SUMMARY

From this discussion it is obvious that no single theory can encompass all the known facts. Furthermore, the importance of different factors undoubtedly varies widely with the individual patient. It must be remembered, too, that profound changes are occurring simultaneously during senescence, so that it is difficult to point to any single alteration as the fundamental etiologic factor. To specify categorically when speaking of a system as complicated as the lens that one alteration gave rise to a second which in turn produced a third is extremely hazardous. In most cases it can be said only that certain abnormal manifestations are usually present together.

The significance of endocrine disturbances in the causation of senile cataract is obscure. Certainly in many cases it seems likely that they play an important if not a decisive role. Many workers⁵ have reported a disturbed sugar metabolism in persons with senile cataract. The blood calcium content is essentially normal in such persons; so hypoparathyroidism would not appear to be an important etiologic factor. Symptoms of a latent tendency to hypoparathyroidism, however, have

134. Vogt, A.: *Lehrbuch und Atlas der Spaltlampenmikroskopie des lebenden Auges: Teil II. Linse und Zonula*, Berlin, Julius Springer, 1931.

been reported in a high percentage of persons with presenile cataract.¹³⁵ It has been suggested that an insufficiency of certain principles of the pituitary gland may aid in the evolution of senile cataract.¹³⁶ The theory of gonadal insufficiency also has its supporters.¹³⁷ Nevertheless, the relation between the endocrine glands and senile cataract remains unsettled. Although the claims of an intimate correlation are stimulating, they are far from convincing. Much experimental and statistical investigation is necessary before a hormonal imbalance can be postulated as a decisive factor.

Senescence is characterized by decreased permeability of cells together with diminished nutrition and impaired excretion of waste products. The lens offers no exception to these general conditions. These three changes are in such intimate collaboration that it is extremely difficult to attribute the pathologic sequelae to any one. In this connection, too, it should be remembered that similar aging processes attack the uveal tissues. Alterations in these structures could affect the lens secondarily by giving rise to inadequacy or derangement of the aqueous humor.

Originally it was thought that senile cataract might be partially attributable to an increased permeability of the capsule with age.¹³⁸ This theory has been refuted by numerous workers, who found that the lens capsules of young animals are more permeable than those of old animals.¹³⁹ Their view has received further confirmation anatomically, for the thickness of the lens capsule increases with age.¹⁴⁰ If even a slight decrease in the passage of vital nutrients or in the removal of toxic

135. Fischer, J., and Triebenstein, O.: Untersuchungen über Tetanie und Alterstar, *Klin. Monatsbl. f. Augenh.* **52**:441, 1914. Greppin, M.: Ueber einen Fall von parathyreopriver Tetanie mit Kataraktbildung und Epithelkörperchentransplantation, *Schweiz. med. Wchnschr.* **52**:1260, 1922. Peters, A.: Zur Pathogenese der Katarakt, *Klin. Monatsbl. f. Augenh.* **43**:621, 1905; footnote 22a.

136. Blatt, N.; Bratianu, S.; Jovin, I., and Milco, S. M.: Katarakta und Hypophyse, *Tr. Internat. Ophth. Cong. (1937) (Endocrinol. et l'œil)* **4**:109, 1938.

137. Fischer-Galati: *Clinique* **24**:119, 1929. Siegrist.¹

138. Löwenstein, A.: Ueber eine neue Theorie des Altersstars, *Klin. Monatsbl. f. Augenh.* **74**:786, 1925; Eine neue Anschauung über die Entstehung des Altersstars, *Arch. f. Ophth.* **116**:438, 1926. Löwenstein, A., and Haurowitz, F.: Experimentelle Untersuchungen über das Verhalten der Rinderlinse bei Veränderung des umgebenden Mediums, *ibid.* **122**:654, 1929.

139. Friedenwald,⁴⁴ Bellows and Chinn,⁸⁷ Gifford, Lebensohn and Punttenney.¹²⁰

140. Salzmann, M.: *The Anatomy and Histology of the Human Eyeball in the Normal State, Its Development and Senescence*, translated by E. V. L. Brown, Chicago, University of Chicago Press, 1912. Fincham: *Tr. Optic. Soc. America* **30**:101, 1929; cited by Duke-Elder, W. S.: *Text-Book of Ophthalmology*, St. Louis, C. V. Mosby Company, 1932, vol. 1.

compounds was maintained for a long period, death of the lens might easily result. Such a possibility is by no means remote in the case of the older patient suffering from widespread impairment of the vital organs.

Appreciation of the importance of a decreased nutrient supply in the pathogenesis of senile cataract will probably increase as knowledge of intracellular respiration broadens. Subclinical vitamin deficiencies maintained for months or years might easily initiate irreversible changes in the lens. Clinicians have shown such conditions to be surprisingly prevalent even at present. Although adequate quantities of the compound may be supplied in the diet, the permeability of the lens capsule may be so altered by toxic, metabolic or traumatic influences or the influence of radiant energy that the essential respiratory systems are lost. Also, alterations in osmotic effect of both electrolytes and non-electrolytes may modify or inhibit the activity of the respiratory substances. With the entire problem of respiratory enzymes now under intensive investigation, much profitable work on this phase of lenticular metabolism may be confidently anticipated.

The extensive literature on toxic substances in the production of cataract presents an imposing case for their role in senile cataract. However, it must be remembered that the compounds discussed are in most cases unphysiologic and will not appear in the body in appreciable quantities. Whether the accumulation of normal metabolic products in abnormal concentrations would produce lenticular changes is unsettled. Since all organs show a diminished efficiency with age, waste products reach considerably higher than normal concentrations. These high concentrations might conceivably have a direct toxic action on the lens or an indirect action due to osmotic effects.

The continual absorption of radiant energy by the lens throughout life may produce changes in its protein structure resulting eventually in opacification. This direct action on the lens might also alter the permeability of the fibers or the various interrelations of the organic and the inorganic constituents contained therein. The known sensitivity of glutathione and riboflavin to light suggests that intracellular respiratory systems of the lens might become impaired after long-continued exposure. Whether such derangements occur to any extent in the adult lens can be determined only by further experimentation. In any event, the relation of radiant energy to senile cataract cannot be casually dismissed.

Osmotic disturbances may also be of fundamental importance in senile cataract. The decrease in renal and in hepatic efficiency with age is well known. Hyperglycemia is common. Nitrogenous waste products are improperly eliminated, and their concentration in the blood is high. Theoretically the accumulation of such compounds in the blood should

act in a manner similar to that of the increase in concentrations following the intravenous injection of hypertonic solutions. Although the effect would be far less marked than that obtained in an experiment producing acute changes, persistent action over long periods might produce the same result.

The rapid biochemical advances of the last few years, especially in the fields of protein structure and of intracellular respiratory enzymes, afford hope that a widespread fundamental change may eventually be observed. Until then, suffice it to say that cataract may in isolated cases result largely from any of the causes discussed but in most instances develops from several such causes progressing simultaneously.

Obituaries

FRANCIS WAYLES SHINE, M.D.

1874-1941

Francis Wayles Shine was born in Orlando, Fla., on June 25, 1874 and died Sept. 24, 1941 at the University of Virginia Hospital, Charlottesville, Va.

Dr. Shine had suffered from high blood pressure for several years, and it was a matter of sincere regret to his many friends when it became necessary for him to give up his work. As he was a great-great grandson of Thomas Jefferson, it seems entirely fitting that he should have settled in Charlottesville, Va., after retiring from active practice in New York. He was buried in the Jefferson Cemetery, on the slope of Monticello Mountain, near the grave of his illustrious ancestor.

He was the son of Thomas J. Shine, a captain in the Confederate Army, and Virginia Epps Shine, a great-grand daughter of Jefferson.

Dr. Shine graduated in medicine from the University of Virginia in the class of 1898, and shortly thereafter he engaged in practice in the city of Boston, where he remained for three years. He then became interested in ophthalmology and went to Vienna and Prague for a year of study. When he returned from Europe, he joined the house staff of the New York Eye and Ear Infirmary for a two and one-half year internship. On completion of this course, he opened an office in New York city and was appointed a member of the attending staff at the New York Eye and Ear Infirmary, where he served successively in the capacity of clinical assistant, assistant surgeon, surgeon, executive surgeon and consulting surgeon and as a member of the board of directors.

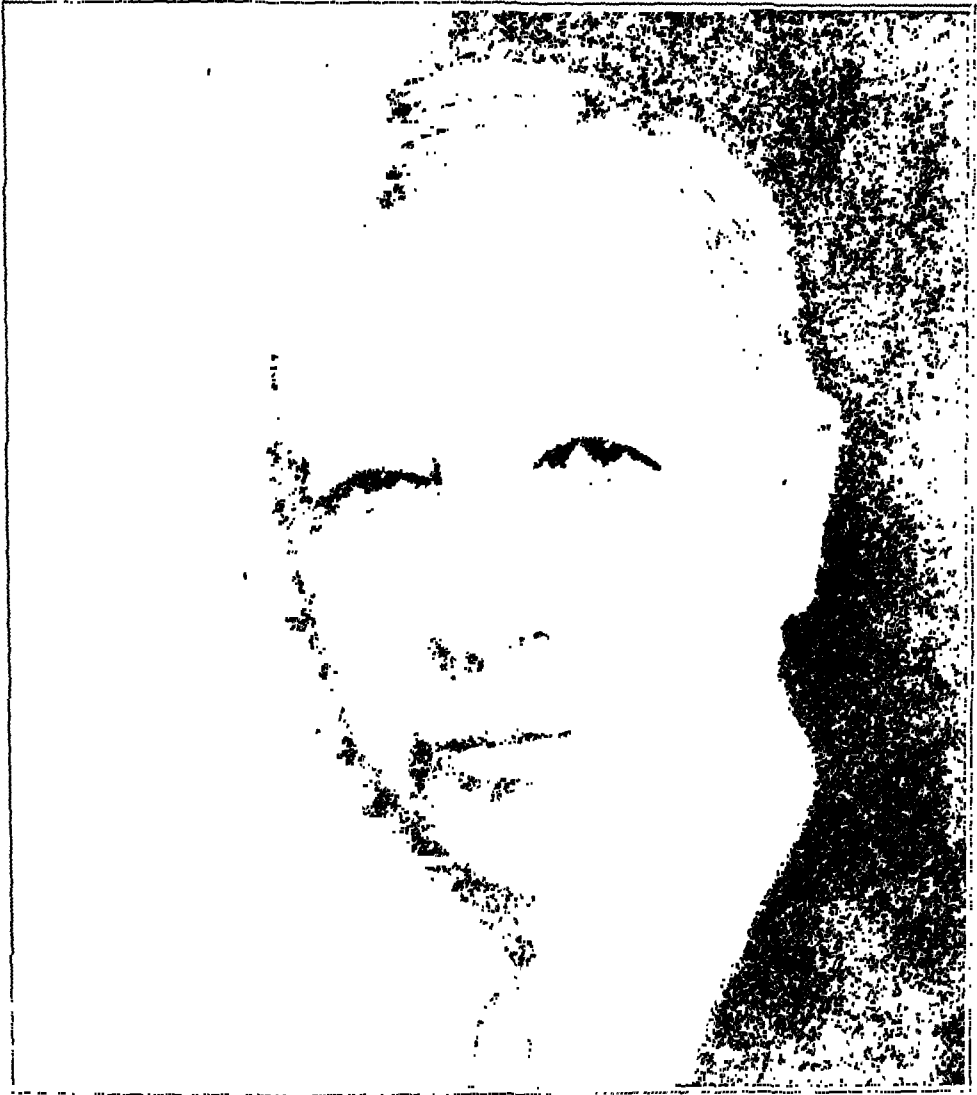
In 1917 Dr. Shine went to France with the rank of captain as a member of an American Expeditionary Force unit formed by members of the New York Hospital. Later he was promoted to the rank of major and was made consultant for all of the American soldiers in the Paris district. He was also consultant to the American Hospital in Paris.

He was a member of the following medical societies: the American Medical Association, American Academy of Ophthalmology and Otolaryngology, American Ophthalmological Society, New York Ophthalmological Society, New York Academy of Medicine and New York State Medical Society. At the time of his death he was consulting surgeon to the New York Eye and Ear Infirmary and consulting ophthalmologist to the New York Hospital.

Dr. Shine was always interested in athletics and played quarterback on the University of Virginia football team in 1893. He was fond of

tennis and golf and was a member of the Racquet and Tennis Club and the Deepdale Golf Club. He also was a member of the Metropolitan Club of New York.

In May 1938 Dr. Shine married Mrs. Edna Wood Bedell, of Charleston, S. C., who survives him, as does his sister, Mrs. Frank B. Stoneman, of Miami, Fla.



FRANCIS WAYLES SHINE, M.D.

1874-1941

Dr. Shine was an excellent clinician and a skilful operator, which won him the respect of his colleagues. He possessed great charm and an agreeable personality combined with loyalty and a high sense of honor. His death is a loss to a large circle of friends and patients.

CLYDE E. McDANNALD.

News and Notes

EDITED BY W. L. BENEDICT

SOCIETY NEWS

Pan-American Congress of Ophthalmology.—The second Pan-American Congress of Ophthalmology will be held in Montevideo, Uruguay, in March 1943.

The Uruguayan Society of Ophthalmology at its meeting held September 12, realizing the importance of this event and conscious of the great honor paid to Uruguay, asked for the collaboration of all its members in the organization of the forthcoming congress.

The following central executive committee was elected: President, Prof. A. Vazquez-Barrière; vice-presidents, Drs. C. M. Berro and W. Isola; treasurer, Dr. J. A. Sicardi, and secretaries, Drs. A. Paiva, R. Rodriguez-Barrios and C. Garbino.

The executive committee has obtained a decree from the government of the republic recognizing the official character of the congress and directing that suitable invitations be addressed to all the American countries by the ministry of foreign affairs.

It has also been resolved to add to the congress a department of social ophthalmology, which will have the same importance as the departments devoted to science. The purpose of this department will be to coordinate the efforts of all the American countries in the great social work of preventing blindness and trachoma.

The executive committee proposes to write to the members of the council, who are delegated in the different countries of the Americas, for the constitution of the national committee of each country and for the addresses of all the ophthalmologists in each country.

American Academy of Ophthalmology and Otolaryngology

Officers Elected.—Dr. James A. Babbitt, emeritus professor of clinical otolaryngology at the University of Pennsylvania School of Medicine and associate professor of otolaryngology in the university's graduate school of medicine, was named president-elect of the American Academy of Ophthalmology and Otolaryngology at its annual meeting, held in Chicago October 19 to 23. Dr. Babbitt will take office Jan. 1, 1943. The present president-elect is Dr. Ralph I. Lloyd, Brooklyn, who will assume office Jan. 1, 1942.

The vice presidents elected are Drs. Walter Theobald, Chicago; Forrest J. Pinkerton, Honolulu, Hawaii, and Francis E. LeJeune, New Orleans. Dr. Secord H. Large, Cleveland, was reelected comptroller and Dr. William P. Wherry, Omaha, executive secretary-treasurer.

Born in Vermont in 1869, Dr. Babbitt graduated at the University of Pennsylvania School of Medicine in 1898. Besides his professorships at his alma mater, he has served on the staff of the Children's Hospital of the Mary J. Drexel Home and as consultant to Lankenau, Children's,

Misericordia and Mercy-Fitzgerald hospitals, in Philadelphia. During World War I he served in France and in Germany with the American Red Cross.

Dr. Babbitt is president of the American Laryngological, Rhinological and Otological Society and in 1939 was president of the American Laryngological Association. He is also a member of the American Otological Society, the American College of Surgeons, the American Medical Association and various Philadelphia organizations. Since 1939 he has been a member of the editorial board of the *Archives of Otolaryngology*.

Awards for Scientific Exhibits.—The awards for the best scientific exhibits, announced October 23, were made in three classifications. For excellence of presentation, Dr. Phillips Thygeson, Presbyterian Hospital, New York, received the award in ophthalmology for his exhibit on infections of the eye and their treatment with sulfanilamide and its derivatives, and Dr. Maurice F. Snitman, University of Illinois College of Medicine, Chicago, the award in otolaryngology for his exhibit on the anatomy of the ear, nose and throat.

The second classification was originality. The award for ophthalmology went jointly to Drs. J. Goldsmith and Henry Minsky, Mount Sinai Hospital, New York, for their presentations on cataract extraction and a method of studying the inner structures of the eye. In the section on the ear, nose and throat the award went to Dr. Paul Holinger, University of Illinois College of Medicine, Chicago, for his work on a new method of photographing the lower part of the respiratory tract, the tracheobronchial tree and the esophagus.

The third group of exhibits were those judged for their teaching value. An award was given to Dr. Peter Kronfeld, Illinois Eye and Ear Infirmary, Chicago, for his studies of tension within the eye and to Dr. Henry B. Orton, Newark, N. J., for an exhibit on cancer of the larynx.

Special mention was given to Philip F. Swindle, Ph.D., Milwaukee, for an exhibit on the blood vessels in the nose and eyes; to Dr. Henry Hilgartner, Austin, Texas, for kodachrome photographs of the background of the eye and the exterior of the eye, and to Drs. Gordon New and John Erich, Rochester, Minn., for demonstrations showing repair of facial injuries.

Specialists Honored.—Dr. Samuel J. Kopetzky and Dr. Conrad Berens, New York, and Dr. Jonas S. Friedenwald, Baltimore, were elected members of the Honor Society of the American Academy of Ophthalmology and Otolaryngology. Dr. L. W. Dean became a member of the Honor Society ex officio. The announcement was made at the annual banquet, held at the Palmer House.

The Honor Society was founded by the academy in 1939 as a tribute to its living past presidents. Now the members may elect to membership by secret ballot any of their colleagues who have given distinguished service to the organization and to the two specialties represented. The society acts as an advisory group to the academy's governing council.

Dr. Kopetzky, president of the Medical Society of the State of New York and director of the medical division of the Selective Service System of the New York city area, has long been active in the field of otolaryn-

gology and in medical organization. He graduated from Columbia University College of Physicians and Surgeons, New York, in 1898 and became an instructor in diseases of the ear at the New York Post-Graduate Medical School and Hospital in 1905. He has been for a number of years professor of otology, New York Polyclinic Medical School and Hospital, and since 1939 has been director of the department of otolaryngology at that school. He is also director of otolaryngology at Israel-Zion Hospital, Brooklyn, and consulting otolaryngologist to the following hospitals: Beth Israel Hospital, New York; Nyack Hospital, Nyack, N. Y.; Newark Beth Israel Hospital, Newark, N. J.; Vassar Brothers Hospital, Poughkeepsie, N. Y., and Jamaica Hospital, Jamaica, L. I., N. Y. Besides the academy, Dr. Kopetzky is a member of the New York Academy of Medicine, the American College of Surgeons and the American Laryngological, Rhinological and Otological Society, of which he was president in 1938, and he has been a member of the House of Delegates of the American Medical Association for many years. He has served in many official capacities in the New York county and state medical societies, is editor of *New York Medical Week* and was for several years on the editorial staff of the *New York State Journal of Medicine* as literary chairman. He served in the United States Army during the Spanish-American War and in the medical corps in World War I, reaching the rank of colonel. He served in France with the 81st Division and was cited for gallantry.

Dr. Berens, who graduated from the University of Pennsylvania School of Medicine, Philadelphia, in 1911, is associate professor of ophthalmology at New York University College of Medicine and chairman of the American Board of Ophthalmology. He is executive secretary for North America of the recently organized Pan-American Congress of Ophthalmology and served as a member of the organizing committee. He is director of research at the New York Eye and Ear Infirmary, directing surgeon and pathologist of the Lighthouse Eye Clinic of the New York Association for the Blind, directing ophthalmologist of the Midtown Hospital and directing surgeon of the Seamen's Church Institute. At various times he has served on the staffs of St. Luke's Hospital, the New York Infirmary for Women and Children and Veterans' Administration Facility No. 81 and as a member of an advisory committee to the Associated Hospital Service of New York. He is the editor of a standard textbook on diseases of the eye and has devised various instruments used in the treatment of these conditions. Among professional societies of which he is a member, in addition to the academy, are the American College of Surgeons, the American Ophthalmological Society and the New York Society of Clinical Ophthalmology. During World War I he served in France.

Dr. Friedenwald has been associate professor of ophthalmology at Johns Hopkins University School of Medicine and visiting ophthalmologist to Johns Hopkins Hospital since 1931. He took his medical degree at Johns Hopkins in 1920 and was appointed an instructor in 1923. He is ophthalmic surgeon to Baltimore Eye, Ear and Throat Charity, Union Memorial, Sinai and Provident hospitals. He is the author of a book entitled "Pathology of the Eye" and a frequent contributor to professional journals. In 1935 the Section on Ophthalmology of the

American Medical Association awarded him the Lucien Howe Medal for research. Professional societies of which Dr. Friedenwald is a member include, in addition to the academy and the American Medical Association, the American Ophthalmological Society, the American Society for Clinical Investigation and the Ophthalmological Society of the United Kingdom.

GENERAL NEWS

Examination for Orthoptic Technicians.—The American Orthoptic Council will conduct two practical and oral examinations for orthoptic technicians in 1942. The first will be held in New York, preceding the Annual Session of the American Medical Association in June. The second will be held in San Francisco, preceding the meeting of the American Academy of Ophthalmology and Otolaryngology in October. There will be only one written examination, which will be conducted throughout the country in May. Applications to take this examination must be received before April 1. Only persons passing the written examination will be eligible to take either of the practical and oral examinations.

Abstracts from Current Literature

EDITED BY DR. WILLIAM ZENTMAYER

Bacteriology and Serology

PRACTICAL VALUE OF ERYTHROCYTE SEDIMENTATION RATE IN OPHTHALMOLOGY. G. v. LUGOSSY, *Arch. f. Ophth.* 142: 16, 1940.

An increased sedimentation rate of the erythrocytes is a nonspecific reaction to localized or systemic diseases which entail increased (toxic) destruction of body proteins. The author reports on 269 determinations of the sedimentation rate made on 114 patients suffering from various ocular and systemic diseases. In general the rate was increased during the acute phase of the ocular disease and its return to normal was parallel to clinical improvement or subsidence of the disease. Repeated determinations indicated whether the disease was progressive or regressive and thus were of prognostic value. In some instances a return of the sedimentation rate to normal indicated a favorable course of the disease before this could be recognized on the basis of the clinical findings. The author says: "In iritis due to focal infection the sedimentation rate does not return to normal until the focus of infection is completely eradicated. In phlyctenular disease a persistently increased sedimentation rate after the ocular attack has subsided foretells recurrences. Repeated determinations during recovery from intraocular operations permit conclusions concerning the probable outcome.

P. C. KRONFELD.

General Pathology

FORMATION OF OSSEOUS TISSUE IN THE CHOROID. A. ZWIAUER, *Arch. f. Ophth.* 142: 68, 1940.

The author takes issue with the view lately expressed again by Samuels (Ossification of the Choroid, *Arch. Ophth.* 21: 545 [March] 1938) that the choroid possesses the specific power of forming bone. New anatomic material from Meller's clinic is presented to show that bone may form in any tissue of the eye if the particular tissue becomes replaced by fibrous tissue which later undergoes regressive changes (diminution of blood supply and disappearance of cells). Ossification occurs rarely in membranes lying on the ciliary body because the regressive changes in the membrane are prevented by the good blood supply of the cyclitic membranes. Several cases of the formation of bone in the areas of the choroid in which fibrous transformation of the choroidal parenchyma had preceded the formation of bone are described in detail and illustrated with photomicrographs.

In summary, there is no reason to assume a specific quality of the choroid to form bone.

P. C. KRONFELD.

Injuries

ENDO-OCULAR FOREIGN BODIES. J. HURTAULT, M. X. LANDO and A. G. QUEROL, Arch. de oftal. de Buenos Aires 14: 576 (July) 1939.

Three cases are reported of cataract following the entrance of a foreign body into the eye.

In the first case the patient presented extensive siderosis with opacification of the lens due to the siderosis and not to any direct injury to the lens. The foreign body was in the posterior segment of the eyeball, and its presence was not recognized until two years after the injury. It was extracted by means of Mulligan's giant electromagnet. Five years later the cataract was extracted in toto. The final vision was 10/10, and the siderosis disappeared.

In the second case the foreign body was lodged in the interior of the lens. It was discovered two months after the injury, and a month later an extracapsular extraction of the lens and the foreign body was performed. The resulting vision was 10/10.

The third case was one of traumatic cataract in which after extraction of the soft matter of the lens and absorption of the remainder a foreign body was discovered implanted near the margin of the iris. Although the vision was 5/10, the authors considered extraction of the foreign body indicated.

C. E. FINLAY.

Lens

TWO CASES OF ANTERIOR LENTIGLOBUS. A. URRETS ZAVALIA and R. OBREGON OLIVA, Arch. de oftal. de Buenos Aires 14: 848 (Sept.) 1939.

Anterior lentiglobus is reported in two brothers. In one the lesion was present in only one eye. The parents were first cousins.

The pathogenesis is discussed without the authors arriving at a definite conclusion.

The paper is illustrated with colored biomicrographs.

C. E. FINLAY.

CONGENITAL ANNULAR CATARACT (RINGSTARLINSE-VON SZILY). A. VÁZQUEZ BARRIÈRE, Arch. de oftal. de Buenos Aires 14: 875 (Oct.) 1939.

A case is reported of an annular cataract such as that described by von Szily.

The patient, 34 years of age, had congenital nystagmus and had had bilateral cataract since birth. The right eye, operated on when he was 18 years old, showed an upward operative coloboma of the iris occupied by a membranous secondary cataract. The vision was reduced to perception of fingers at 1 meter. There was bilateral horizontal nystagmus of a pendulum type. In the left eye, the vision of which was scarcely perception of fingers at 0.5 cm., the pupil was dilated and irregular and the lens was subluxated upward and inward and was completely opaque and white, with a uniform calcareous aspect. The lens had in its center a circular opening 3 mm. in diameter leading to a tunnel 2 mm.

in depth, with irregular excavations into the calcareous substance, the bottom of which was closed by a lead-colored membrane. When this eye was operated on, liquefied vitreous immediately exuded and the lens was extracted by means of a Weber loop. After one month vision equaled 0.1. No histologic examination was possible. The author reviews different varieties of cataract described by von Szily. The type under consideration is attributed by the latter to an axial degeneration.

C. E. FINLAY.

Lids

TREATMENT OF BLEPHARITIS WITH CASTOR OIL. I. SMELIANSKY, *Vestnik oftal.* 17: 134, 1941.

After having tried all known remedies for the blepharitis from which he had suffered since childhood, Smeliansky tried castor oil. Three daily applications to the lid margins gave unexpectedly quick relief. He then used castor oil a few times weekly for prophylaxis. He appeals to ophthalmologists to try this inexpensive and simple remedy in a large number of cases of chronic squamous blepharitis.

O. SITCHEVSKA.

Methods of Examination

THE EXPERIMENTAL RADIOGRAPHY OF SMALL FRAGMENTS OF GLASS IN RELATION TO THE HUMAN EYE. R. U. GILLAN, *Brit. J. Ophth.* 25: 117 (March) 1941.

Gillan states the following conclusions drawn from his experimental work:

"(1) That most kinds of glass in common use are opaque to X-rays.

"(2) That small fragments of the order of $\frac{1}{2}$ -2 mm. in thickness show an opacity when exposed through the thickness of the eye and eyelids, and in addition through the thickness of the skull, but that fragments under 1 mm. in thickness may be difficult of detection in such conditions.

"(3) It may be concluded that pieces of glass actually in the eye or orbit and exposed to X-rays under comparable conditions would also show, but that having regard to the somewhat greater distance of the foreign particles from the film in such a case, fragments of under 1 mm. in thickness would a fortiori, be difficult of detection."

W. ZENTMAYER.

A NEW DARK ADAPTATION TESTER. S. YUDKIN, *Brit. J. Ophth.* 25: 231 (May) 1941.

Yudkin describes an instrument for testing dark adaptation. The method of use and advantages over other instruments are discussed.

The advantages claimed are that both "bleaching" and testing are carried out with the same instrument. The bleaching tube insures that the whole retina is bleached. The test objects can be varied, so that the subject's statements can be verified. The polaroid screens allow fine adjustment of the illumination.

The article is illustrated.

W. ZENTMAYER.

ENTOPTIC PHENOMENA. E. P. FORTIN, Arch. de oftal. de Buenos Aires 14: 917 (Oct.) 1939.

Since the time of Helmholtz two methods have been used in the entoptic observation of the retinal vessels. One is based on the movement over the sclera of a luminous ray condensed by a short focus lens and the other on movement before the eye of a lamp. The author refers to another method, that of utilizing a stenopaic hole and the blue rays of a mercury vapor lamp.

After calling attention to the defects of the first methods, he describes an improvement on the third in which a small arc lamp with a reddish yellow filter of the same color as the ocular fundus is used, the heat rays being eliminated by passage through a vessel containing water.

C. E. FINLAY.

Ocular Muscles

ETIOPATHOGENESIS OF STRABISMUS. J. MALBRAN, Arch. de oftal. de Buenos Aires 14: 771 (Sept.) 1939.

This is a lengthy paper in which the author reviews the current opinions on strabismus and discusses in succession and in great detail the influence of various general etiologic factors, such as sex, age, heredity, neuropsychiatric disturbances, infectious diseases, fever and traumatism, and three types of ocular etiologic factors: (1) those due to an anomalous position of the eyes in a state of rest and resulting from alterations in size and in form of the orbits and of the eyeballs, from conditions inherent in the retrobulbar structures and from anomalies in the ocular muscles, their fasciae and their aponeurotic expansions; (2) those arising from irregularities in the optic impressions received by each eye and due to lesions in the media, the retina and the optic nerve, to ametropia and to aniseikonia, and (3) those originating in functional disturbance of the muscular mechanism in convergence and accommodation, with a defect or absence of fusion, and in pathologic lesions of the vestibular apparatus.

The following conclusions are stated: The child from birth or from the first weeks of life can fix with both maculas an object or point within his visual field which has attracted his attention. This reflex of retinal correspondence the author calls "motor" fusion. He accepts in consequence the capacity for fixation of corresponding areas of the two retinas, with an equivalent special spatial projection, as innate and involuntary. On the other hand, he considers "sensorial" fusion as necessarily acquired. The anatomic factors are what first lead to positional anomalies combined or not with those due to innervation. The author does not accept weakness in fusion as a predominant factor in squint, although he states that it may have an influence. If the lesion of the anatomic positional factors which leads to the strabismus occurs before fusion has been established the result will be anomalous retinal correspondence; if, on the other hand, fusion has already reached a certain development, the normal congenital correspondence will persist in spite of the motor anomaly. He does not believe that divergent squint is always due to a defect in fusion; in some cases, in which the squint appears early and is accompanied by familial or hereditary factors, such

a defect may be the cause, but in most cases squint is due to an alteration in the anatomic factors. In vertical strabismus positional anomalies constitute the predominating factor. Ohm's oblique squint and the sursumduction squint of Cords, termed by Bielschowsky "hyperfunction of the inferior oblique muscle," may be due to a variety of causes. In many cases it has been preceded by paralysis of the superior oblique muscle; in others the vestibular apparatus plays an important role, and in others the insertion of the internal rectus muscle is abnormal (Cords).

C. E. FINLAY.

Parasites

FIRST DEMONSTRATION IN SWITZERLAND BY MEANS OF THE SLIT LAMP OF NUMEROUS MICROFILARIA IN BOTH EYES: REPORT OF A CASE. B. SEMADENI, *Klin. Monatsbl. f. Augenh.* 104: 417 (April) 1940.

A geologist aged 36 who was active in Africa for two years was troubled with slight conjunctival congestion, cutaneous eruptions resembling herpes zoster on his forehead, swelling and induration on his left ear and on his nose, a digestive disorder, palpitation of the heart, fatigue, dyspnea and nervousness. The variety of symptoms led to the diagnosis of hysteria. Examination with the slit lamp showed numerous corneal foci, in larger accumulation toward the limbus. They were observed mostly under Bowman's membrane but also in the corneal parenchyma. The foci consisted of nests of the larval form of *Onchocerca volvulus* in the eyes and in the skin. About 300 of the microfilarias were supposed to have been present in one cornea. Isolated filarias were found in the anterior chamber. The transmission to human beings occurs by a fly, *Simulium damnosum* (Leuckart). No therapeutic means are known, but the prognosis is favorable. The parasites die within about eight years. Protection of the eyes by tinted glasses is recommended. References to the literature are given, and the paper is illustrated with photographs taken with the aid of a slit lamp.

K. L. STOLL.

Refraction and Accommodation

IS MYOPIA A DEFICIENCY DISEASE? H. MILLER, *Am. J. Ophth.* 23: 296 (March) 1940.

From questionnaires sent to both myopes and hyperopes as to eating and other habits and from experiments on rats Miller gives the following summary and conclusion:

"A large percentage of myopic people are prone to discard fats and other essential foods from their diet. At least 8 per cent of fat in the diet is essential for health and growth because of the vitamin A these fats contain and also as a solvent for carotenes. Clinical and experimental evidences are produced to show that myopia is found where such food elements are lacking in the diet. Therefore, in answering the question, 'Is myopia a deficiency disease?' it appears not unreasonable to conclude that myopia is largely due to dietary deficiency."

W. S. REESE.

OSMOTHERAPY IN HIGH MYOPIA. V. P. FILATOV and A. E. VOLOKITENKO, *Vestnik oftal.* 17:515, 1940.

Filatov and his assistants have been using osmotherapy in the treatment of various diseases of the eye since 1933. The basis of osmotherapy is the transudation of cellular liquid into the blood and the suction of toxic substances from the inflammatory focus; these toxic substances may stimulate the organism and produce antibodies, ferments, catalyzers, etc. The endothelium plays an important role in osmotherapy because it increases the secretory function of the body.

Fourteen patients having 26 eyes with high myopia without retinal changes were treated by intravenous injections of 10 per cent of chemically pure salt solution; the dose was 10 cc. every other day for about 15 injections. In 21 eyes there was considerable improvement of vision, and in 5 there was no change. Eight patients showed an enlargement of the visual fields.

O. SITCHEVSKA.

Retina and Optic Nerve

SYPHILITIC PRIMARY OPTIC ATROPHY. J. E. MOORE and A. C. WOODS, *Am. J. Ophth.* 23:145 (Feb.) 1940.

Moore and Woods discuss the frequency of syphilis as a cause of primary atrophy of the optic nerve; the visual fields in this disease; early diagnosis, especially as related to dark adaptation, and the effect of various kinds of treatment. Detailed studies of their clinical findings are to be presented later.

W. S. REESE.

THE PATHOGENESIS OF RETINITIS PIGMENTOSA (SCLEROSIS PIGMENTOSA CHORIORETINALIS). L. LEVY-WOLFF, *Am. J. Ophth.* 23:275 (March) 1940.

It is concluded that disturbed vasomotor regulation is the causal damaging factor in retinitis pigmentosa and that the disease is characterized by two general symptoms, hypotony and lowering of the temperature. The hypothalamus is pointed out as the site of the disturbance. Cholesteremia is reported as a constant finding and the assumption made that it influences the temperature probably by action on the walls of the vessels.

W. S. REESE.

THE PATHOGENESIS OF RETINITIS PIGMENTOSA (SCLEROSIS PIGMENTOSA CHORIORETINALIS). L. LEVY-WOLFF, *Am. J. Ophth.* 23:418 (April) 1940.

This rather long and interesting article does not lend itself to abstracting. The author thinks that sclerosis pigmentosa chorioretinalis, as she prefers to call it, is the manifestation of a circulatory disorder actuated by the central nervous system and that it first attacks the choriocapillaris. Later the retinal end system also becomes affected. She believes that the ganglion cells of the brain are undoubtedly involved similarly to those of the retina and that the juvenile form of amaurotic family idiocy may pertain to sclerosis pigmentosa chorioretinalis. This is the continuation of a previous article.

W. S. REESE.

THE FUNDUS IN ACUTE RETROBULBAR NEURITIS. F. FISCHER, Klin. Monatsbl. f. Augenh. 104: 145 (Feb.) 1940.

The author reports his observations on 100 patients with acute retrobulbar neuritis, 50 men and 50 women. He excluded patients who showed complications due to the effects of toxins, including nicotine and alcohol, on the optic nerve; Leber's hereditary atrophy of the optic nerve; so-called chronic retrobulbar neuritis, and neuritis caused by tumor of the brain. Only 25 men appeared for treatment in the period during which 50 women were admitted for treatment. The fundus was normal in only 16 patients, whereas edema of the disk was present in 62. This fact is contradictory to the experiences published by other writers, who declared that neuritis and choked disk occur rarely in association with acute retrobulbar neuritis. Multiple sclerosis was the cause of the acute retrobulbar neuritis in most of the cases described by other writers and in one third of Fischer's cases; no cause was established in 10 of his cases.

The frequency of edema of the disk observed by Fischer in association with acute retrobulbar neuritis and with multiple sclerosis prompts him to the opinion that a correlation exists between these two phenomena. In fact, multiple sclerosis may have been the cause of acute retrobulbar neuritis in many cases in which the origin remained hidden.

K. L. STOLL.

GENESIS OF TRAUMATIC ANGIOPATHY OF THE RETINA (PURTSCHER):
REPORT OF A CASE. A. M. BRUHN, Klin. Monatsbl. f. Augenh.
104: 152 (Feb.) 1940.

Referring to cases in point, the author reports the case of an aviator who fell from the rigging of his plane to water 5 meters below. Aside from a fracture of the nose he complained of a central visual obscuration in his right eye immediately after the accident. Examination ten days later showed vision in the right eye reduced to 1/10. The fundus presented the picture of traumatic angiopathy of the retina; edema of the macula corresponded to the central scotoma. Fine white dots near the veins in the neighborhood of the disk and some isolated linear hemorrhages were noted. The course was unlike that in Purtscher's case, for degeneration of the macula developed, coupled with further reduction of vision. Recovery followed slowly, and fine pigmented spots remained even after restitution of normal vision, three months later.

Bruhn explains the mechanism of the ocular lesion as follows: The man, a perfect swimmer, hit the water feet first. Coming up under his plane, he knocked his nose against it. While he was swimming under water with his mouth closed the compression of his thorax caused a sudden afflux of blood into the periphery. The result was an extravasation of serum from the retinal veins.

K. L. STOLL.

HEMERALOPIA IN COMBATANTS. K. VOM HOFE and M. GLEES, Klin. Monatsbl. f. Augenh. 104: 369 (April) 1940.

The black-out in the cities of Germany drew the attention of physicians to retarded and diminished dark adaptation. Experiences from the

last war were published by A. Jess (*Nachtblindheit mit besonderer Berücksichtigung der während des Krieges gesammelten Erfahrungen, Zentralbl. f. d. ges. Ophth.* 6: 1 and 113, 1921). Vom Hofe and Glees undertook to establish a normal curve of dark adaptation as a standard which would be indispensable in evaluating the condition of soldiers and other persons suffering from disturbed adaptation. The light adaptation was tested with Trendelenburg's apparatus for five minutes and with the dark adaptometer. The normal curve is marked with a heavy line in the charts which illustrate the article. The wide scope of the curves indicating diminished adaptation was divided to indicate night blindness of a minor degree, which is irrelevant in military service, and night blindness of a considerable degree, which causes a reduction of fitness. One hundred soldiers complaining of difficulty of adaptation in dusk or in darkness were examined in order that a more exact distinction might be established between the minor and the considerable degree of this ailment. The authors arrived at the following conclusions: Night blindness of considerable degree exists in men who show a sensitivity of only 5,000 after being at the Engelking-Hartung adaptometer for thirty minutes. Those for whom the value is 6,000 to 10,000 after thirty minutes present a somewhat diminished adaptation which does not necessarily make them unfit for active service. One-eyed men and men with a high degree of amblyopia belong to this group. Malingerers were rarely met with and readily found out. Among 40 soldiers who experienced difficulty of orientation in the dark, 30 referred to members of the family with a similar complaint. Incidentally, 6 men had retinitis pigmentosa of some type and 18 had coloboma of the iris or the choroid, ectopia of the lens, atrophy of the optic nerve, nystagmus, opacity of the vitreous or other disturbance. Unilateral amblyopia was present in 18 men and bilateral amblyopia in 16. Myopia, the degree of which played no role in this research, was observed in 40 men. The influence of a deficiency of vitamin A was questionable, as the men examined had not undergone excessive exertions and were properly nourished. Every recruit should be questioned regarding his adaptation, and those who answer that it is not good should be thoroughly examined.

K. L. STOLL.

TRAUMATIC DETACHMENTS OF THE RETINA. J. C. HOLST, *Acta ophth.* 18: 190, 1940.

Three cases are briefly reported to illustrate the difficulty of appraising the role of trauma in producing detachment of the retina. In order to examine this role further, the author studied a series of 47 eyes with retinal detachment in which an injury may have been a causal factor. He divides these eyes into three groups: (1) 7 in which detachment followed penetrating injury of the globe, (2) 24 in which it followed a nonpenetrating injury of the globe and (3) 16 in which it followed a blunt injury of the skull or came on after severe muscular exertion.

After a detailed analysis of these eyes the author concludes that a perforating injury may cause retinal detachment in a previously healthy eye. The detachment may appear at once or may follow secondary cicatricial contractions later on. A nonpenetrating injury acting directly

on the eyeball can also give rise to a retinal detachment in an eye with no apparent predisposition thereto. The detachment usually follows immediately after the injury, although occasionally there is a latent period. In regard to the third type of etiologic factor, the most difficult to analyze, it is unwise to be dogmatic. It appears, however, that indirect trauma rarely causes detachment unless the eye is predisposed thereto as a result either of myopia or of degenerative changes.

O. P. PERKINS.

RETINAL DETACHMENT IN APHAKIA. J. C. HOLST, *Acta ophth.* 18: 204, 1940.

Among 293 eyes with retinal detachment observed in the Oslo Eye Clinic between 1932 and 1939, 20 were aphakic. A great many complicating factors make it difficult to draw conclusions from a study of these eyes. The author believes it fair to say, however, that the danger of retinal detachment is no greater after intracapsular extraction of an uncomplicated cataract than it is after extracapsular extraction. Holes or tears in the retina were found in all eyes in which it was possible to see the fundus. Sixteen eyes were operated on, of which only 5 were healed.

O. P. PERKINS.

Trachoma

SOME OBSERVATIONS ON THE USE OF SULFANILAMIDE IN TRACHOMA AND ASSOCIATED OCULAR CONDITIONS. W. D. SPINING, *Am. J. Ophth.* 23: 271 (March) 1940.

Spining gives the following summary:

"Fifteen adults with chronic trachoma associated with other acute eye conditions, such as bulbar conjunctivitis, phlyctenular conjunctivitis, and corneal ulcers, recovered rapidly from the acute manifestations under sulfanilamide therapy. In none of these cases, however, was there any evidence that the underlying trachoma was cured or even greatly improved.

Seventeen children between the ages of 8 and 14 years, with chronic trachoma and little or no bulbar or corneal involvement other than slight pannus, were treated with sulfanilamide for periods of 7 to 24 days. Only one clinical cure was obtained. The other 16 showed slight to moderate improvement. The nine patients who received treatment for 21 to 24 days showed no more improvement than those whose treatment was stopped on the seventh day."

W. S. REESE.

TRACHOMA IN JAPAN. H. SHIGA, *Am. J. Ophth.* 23: 306 (March) 1940.

Shiga examined about 14,000 school children of thirteen elementary schools in Kyobashi Ward, Tokyo. He discusses his findings under the following headings: correlation between trachoma and folliculosis, prognosis of trachoma and other types of conjunctivitis, investigation of Prowazek-Halberstaedter bodies and their etiologic significance and treatment of trachoma with special reference to public health admin-

istration. He concludes that the problem of the eradication of trachoma can be solved by public health agencies even though the causation of the disease is not entirely clear.

W. S. REESE.

SULFANILAMIDE AND NEOPRONTOSIL [AZOSULFAMIDE] IN THE TREATMENT OF TRACHOMA. R. D. HARLEY, A. E. BROWN and W. E. HERRELL, *Am. J. Ophth.* 23:662 (June) 1940.

After reporting 11 cases Harley, Brown and Herrell give the following summary and conclusion:

"Eleven cases of trachoma treated by sulfanilamide or allied compounds have been reported. In each case marked objective and subjective improvement occurred. Four of the 11 patients were found to be intolerant to sulfanilamide. In three of these cases treatment with neoprontosil [azosulfamide; disodium 4-sulfamidophenyl-2'-azo-7'-acetyl-amino-1'-hydroxynaphthalene-3'6'-disulfonate] was substituted for sulfanilamide, with apparent continuation of the good results.

"Trachoma in stages II and III seems to make the best response to treatment. Trachoma probably falls into the group of diseases in which low or moderately low concentrations of sulfanilamide in the blood (3 to 5 mg. per 100 cc.) are sufficient to give satisfactory results when maintained for about three weeks. Neoprontosil (oral), because of its low toxicity, lends itself well to the treatment of trachoma when rather prolonged therapy is necessary. It appears to be tolerated in some cases in which an intolerance for sulfanilamide has been found. Although the results of treatment with neoprontosil are not nearly so dramatic, we feel that on prolonged treatment with this drug in trachoma the results will compare favorably with those of sulfanilamide although sulfanilamide appears to be the preferable drug. Our results agree completely with the earlier reports on the use of sulfanilamide in the treatment of trachoma."

W. S. REESE.

ORGANIZATION OF THE ANTITRACHOMA CAMPAIGN IN THE NORTH OF SANTA FÉ (ARGENTINA) IN 1938. J. M. ZAVALIA, *Arch. de oftal. de Buenos Aires* 14:882 (Oct.) 1939.

This is a detailed and complete report of the work against trachoma done in the province of Santa Fé, with full statistical data from different sections and a study of the causation of the different varieties of trachoma. Contributing factors in dissemination of the disease were familial infection, early contamination, ignorance, lack of hygienic precautions and promiscuity.

C. E. FINLAY.

. Tumors

HEMANGIOMA OF THE ORBIT. A. E. MEISENBACH JR., *Am. J. Ophth.* 23:286 (March) 1940.

Meisenbach gives the following summary:

"Six cases of hemangioma of the orbit are reported: one a simple hemangioma; one a simple hemangioma of the lacrimal gland; one a cavernous hemangioma; one a simple hemangioma with considerable

proliferation of endothelial cells; another a fibrohemangioma, composed mostly of thick-walled arteries and veins; and the last, a hemangio-endothelioma composed mostly of blood vessels with thickened walls.

"The last two growths are unique in ophthalmic pathology, being composed of thick-walled vessels in greater number than capillaries. We have been unable to find reports of any similar growths of the orbit in the literature.

"It is interesting that one individual did not appear for removal of the tumor until 63 years of age and another not until 43 years of age. Four of the six tumors were not encapsulated."

W. S. REESE.

NEUROGENIC ORIGIN OF CHOROIDAL SARCOMA. O. W. LEOPOLDSBERGER, *Arch. f. Ophth.* 142: 229, 1940.

From a study of the topographic relations between choroidal sarcoma and the ciliary nerves in 7 cases G. Dvorak-Theobald (Neurogenic Origin of Choroidal Sarcoma, *ARCH. OPHTH.* 18: 971 [Dec.] 1937) concluded "that these tumors originated from the Schwann sheath cells of the posterior ciliary nerves in their passage through the choroid." Leopoldsberger takes issue with this interpretation. In his opinion the histologic observations reported by Dvorak-Theobald do not prove the neurogenic origin of the choroidal sarcoma but only illustrate the well known fact of invasion of ciliary nerves by this sarcoma. Large tumors of this type do not permit conclusions as to their origin, and only study of the smallest sarcomas can give clues with regard to the tissue elements from which the neoplasm is derived. Leopoldsberger does not deny the possibility of a neurogenic origin of certain choroidal tumors. In an eye which had not been examined in vivo he discovered accidentally a flat choroidal neoplasm which measured 5.5 by 8 mm. and was situated temporally to the disk. A long posterior ciliary nerve ran through the neoplasm. In its course through the sclera and the suprachoroidea this nerve was perfectly normal. In the neoplasm, however, a continuous transition from normal nerve cells into tumor cells with the characteristics of aggressive infiltrative growth could be observed. The author concludes that "although even this case is not irrefutable proof of the neurogenic origin of the choroidal sarcoma, it at least renders this concept very probable." The neoplasm present in this eye was so atypical in many respects that it suggests the neurogenic origin of only a small group of choroidal sarcomas (leukosarcomas made up of small spindle cells).

An intimate topographic relation between small sarcomas located in the suprachoroidea and the ciliary nerves was observed in several cases of multiple choroidal sarcomas (Fuchs, E.: *Ueber Sarkom der Aderhaut nebst Bemerkungen über Nekrose der Uvea*, *Arch. f. Ophth.* 77: 326, 1910). In discussing a case of atrophy of the bulb with diffuse chorioretinitis in which an otherwise normal long posterior ciliary nerve in the region of the equator was transformed for about 3 mm. into a spindle-shaped neoplasm highly suggestive of infiltrative growth, Meller many years ago expressed belief in a neurogenic origin of the neoplasm.

In summary, the neurogenic origin of certain unpigmented choroidal sarcomas is definitely within the realm of possibilities. Histologic evi-

dence for the neurogenic origin can be obtained only through the study of very small sarcomas, of which several examples are cited. These tumors were located in the suprachoroidea and had caused no clinical symptoms.

P. C. KRONFELD.

CONJUNCTIVAL LYMPHOMA. J. P. JENSEN, *Acta ophth.* 18: 67, 1940.

Large, long, fairly hard grayish red tumors developed in the conjunctival fornices of a 32 year old man. He had previously undergone operations for the removal of greatly hypertrophied tonsils and of enormous quantities of lymphoid tissue from the rhinopharynx. There was no enlargement of liver or spleen, and examination of the blood and bone marrow revealed no abnormalities. Later, glandular swellings appeared in the neck, axillas and inguinal regions. Microscopic examination of the excised tumors revealed a perfectly uniform tissue consisting of a fine reticulum and enormous numbers of lymphocytes. Lymphosarcoma is regarded by the author as the probable diagnosis.

O. P. PERKINS.

Uvea

ESSENTIAL ATROPHY OF THE IRIS. B. RONES, *Am. J. Ophth.* 23: 163 (Feb.) 1940.

A case of essential atrophy of the iris is reported, the results of pathologic examination are described and the following conclusions are drawn:

"It is obvious in viewing these theories that there is no definite basis for the majority of them. As to the causes of the initial iris atrophy, virtually nothing is elucidated from either the microscopic or the clinical reports cited. The theories are purely speculative and obviously do not explain the condition. Concerning the glaucoma, the blocking of the chamber angle by the dense anterior synechiae easily explains this complication. I do not see the necessity for assuming that the disappearance of the capillary bed of the iris plays a role in the increased intraocular tension, for many cases have been seen clinically in which large areas of the iris were removed as a result of trauma or operative procedures, without a resultant rise of pressure."

W. S. REESE.

OUTCOME OF IRIDOCYCLITIS. A. MIKLÓS, *Arch. f. Ophth.* 142: 203, 1940.

The outcome of anterior uveitis was studied statistically in a group of 500 cases observed in the ophthalmic clinic of the University of Debrecen (Hungary). The uveitis was attributed to tuberculosis in 48 per cent, to syphilis in 15 per cent, to rheumatic infection in 7 per cent, to dental infection in 1.6 per cent and to acute infectious diseases in 3.8 per cent, whereas in 18 per cent no clue with regard to the causation could be found. In 40 per cent the iridocyclitis was of the chronic type. The period of observation varied from one to sixteen years; the average was not stated. The author's criterion of unfavorable prognosis was a final visual acuity of less than 10/200. In his series the vision finally became reduced to less than 10/200 in 15 per cent of all cases and to

less than 20/80 but more than 10/200 in 13 per cent of all cases. In 80 per cent of the cases in which the vision was less than 10/200 the uveitis was diagnosed as tuberculous. Secondary glaucoma occurred in 12 per cent of cases and complicated cataract in 1.8 per cent. In the cases of tuberculous iridocyclitis the response to surgical intervention (iridectomy) was on the whole unfavorable.

Irrespective of the cause, the prognosis of acute iritis was favorable. The author says: "They [patients with acute iritis] are usually well without appreciable loss of vision within three to four weeks. They respond well to treatment and are relatively free of recurrences." Almost 50 per cent of the patients remained free of recurrences for periods varying from one to sixteen years; the average was not stated.

The author states that in cases of uveitis due to syphilis, dental infection or systemic infectious disease the prognosis was in general favorable. In cases of rheumatic iritis iridectomy seemed to have a marked beneficial effect.

With regard to the acute uveitis following intraocular operations the author refers to a paper by Szinegh, of the same clinic, in which encouraging results obtained with chemotherapy were reported. Maklós says: "The iridocyclitis which develops a few weeks after an intraocular operation is usually very stubborn. In some cases it takes a malignant course similar to that of tuberculous iridocyclitis and leads to blindness despite any conceivable form of treatment."

In summary, the prognosis of uveitis is largely dependent on the causation.

P. C. KRONFELD.

TERMINATION OF TUBERCULOUS UVEITIS. G. STROMBURG, *Klin. Monatsbl. f. Augenh.* 104: 384 (April) 1940.

Stromburg examined 500 patients with tuberculous uveitis treated at the ophthalmic clinic of the University of Freiburg from 1900 to 1930 with a view to establishing the termination of recurring intraocular tuberculosis. Of these patients 170 could be interviewed, 126 women and 44 men. The period of observation varied from ten to more than forty years. Both eyes were involved in 160 of the 170 patients, whereas the process remained unilateral in 5 men and 5 women. According to this observation 95 per cent lost vision in both eyes in the course of years or of decades. The onset took place in the second or third decade independently of puberty but followed childbirth in many cases. A relation was noted between menstruation and recurrences. Only 40 of the 170 patients experienced no recurrences for many years; 25 per cent had normal vision after the process was considered cured. Fifty per cent of the eyes were blind, and 70 per cent were lost as a result of secondary glaucoma. The prognosis was unfavorable as soon as increased intraocular tension became evident unless a permanent decrease was obtained. Antiglaucomatous operations, such as broad iridectomy and transfixion, were successful on 30 per cent of 106 eyes. The prognosis was unfavorable in a group of patients in whom every organ of the eye became destroyed by tuberculosis in the course of years. Iridocyclitis was followed in 23 patients by sudden attacks of episcleritis, papillitis and periphlebitis. The process terminated with

phthisis of the eyeball in 65 per cent of the diseased eyes. Fifteen of the patients concerned had had scrofulosis in their youth. Only 5 patients who had scrofulosis early in life experienced no recurrence in the course of several decades. This observation prompted the author to the view that ocular scrofulosis in youth may predispose to severe ocular tuberculosis in later years. Cyclitis, beginning and proceeding in a mild form, mainly in females, may terminate in secondary glaucoma and phthisis after many years.

K. L. STOLL.

Society Transactions

EDITED BY DR. W. L. BENEDICT

AMERICAN MEDICAL ASSOCIATION, SECTION ON OPHTHALMOLOGY

ALBERT C. SNELL, M.D., *Chairman*

DERRICK VAIL, M.D., *Secretary*

Ninety-Second Annual Session, Cleveland, June 4-6, 1941

Some Principles of Medical Ethics and the Practice of Ophthalmology.

Chairman's Address. DR. ALBERT C. SNELL, Rochester, N. Y.

The principles of medical ethics are just as binding on physicians practicing ophthalmology as they are on all other members of the medical profession. There are, however, some situations which are peculiar to the special practice of ophthalmology. These situations present unusual temptations to violate the best ethical standards. When the ethical principles and ideals of the medical profession are not respected by even a small group of ophthalmologists, opprobrium is placed on all the members of the profession, the ethical and the unethical alike. Every individual ophthalmologist becomes the object of derision.

In a booklet published by the American Medical Association the fundamental principles which should activate the relation between the physician and his patients is stated thus: "A profession has for its prime object the service it can render to humanity; reward or financial gain should be a subordinate consideration. It is unprofessional to accept rebates on prescriptions or appliances, or perquisites from attendants who aid in the care of patients."

The following resolutions were adopted by the Section on Ophthalmology of the American Medical Association at the Annual Session in Chicago in June 1924. These, however, were not presented to the House of Delegates.

Resolved, That it is the sense of the Section on Ophthalmology of the American Medical Association that we deprecate the selling of glasses by the ophthalmologist to his patients in communities where the services of reliable dispensing opticians are obtainable.

Resolved, That the acceptance of commissions or considerations, either directly or indirectly, from opticians and optical houses, from the sale of glasses, is absolutely contrary to all our standards of medical ethics, and is just as reprehensible as the splitting of fees.

These principles and resolutions present the obligations which the medical profession regards as the minimum ethical standards of practice

for ophthalmologists. From the information I have been able to gather I fear that these standards are more "honor'd in the breach than the observance."

The situation peculiar to the ophthalmologist consists in the fact that the correction of errors of refraction constitutes a large percentage of his practice—from 60 to 90 per cent—and ophthalmic lenses and their mountings must be supplied and properly fitted to each patient when a correction is prescribed. This requires some form of commercial relation with the nonmedical men who render this service.

There are six methods of supplying glasses:

1. The first method is that in which the ophthalmologist gives the prescription for the lenses directly to the patient, who is instructed to have it filled by any reliable optician of his own choice.

2. By the second method the ophthalmologist personally furnishes the glasses.

3. By the third method the prescription is filled and the mounting completely fitted by a wholesale dispensing optician, who charges a nominal fee for the extra service of adjustment of mountings and collects the prevailing retail price for the completed work.

4. By the fourth method the ophthalmologist sends the patient to some chosen optician, who completes the entire work of filling the prescription, mounting the lenses and adjusting the glasses and collects the full retail price, returning to the ophthalmologist a specified rebate, without the knowledge of the patient.

5. The fifth method is one in which ophthalmologists partially or completely own an optical dispensing store, which at times is designated by the more subtle name of laboratory.

6. There is a sixth method. A few physicians with little knowledge of ophthalmology contract for their services on a salary or on a percentage basis to some retail establishment where both the examinations and the sales are conducted.

The first method is the ideal, ethical one; its employment is in harmony with the resolution of this section. It removes the possibility of any selfish interest or bias in the transaction of supplying glasses. This is the highest ethical form of practice and is followed by the leading ophthalmologists in the United States.

Traumatic Changes in the Retina, Choroid, Nerve Head and Vitreous (Lantern Demonstration). DR. ARTHUR J. BEDELL, Albany, N. Y.

The author presented a large number of kodachrome lantern slides illustrating a variety of lesions of the fundus. He called attention to essential points of differentiation between traumatic and nontraumatic lesions.

Lime Burns of the Eye: Use of Rabbit Peritoneum to Prevent Severe Delayed Effects; Experimental Studies and Report of Cases (Lantern Demonstration). DR. ALBERT LOUIS BROWN, Cincinnati.

This article was published in full, with discussion, in the November issue of the ARCHIVES, page 754.

Retinal Phlebosclerosis (Lantern Demonstration). DR. GLEN GREGORY GIBSON and DR. LAWRENCE W. SMITH, Philadelphia.

This article was published in full, with discussion, in the November issue of the ARCHIVES, page 840.

Retina in Systemic Vascular Hypertension: A Clinical Study of the Caliber of the Retinal Arterioles and the Retinal Arterial Diastolic Blood Pressure. DR. FERDINAND L. P. KOCH, New York.

This article was published in full, with discussion, in the October issue of the ARCHIVES, page 565.

Causes of Blindness in Pennsylvania: An Analysis of the Blindness in over Thirty Thousand Eyes. DR. ALFRED COWAN and BERNICE C. ENGLISH, Philadelphia.

This article was published in full, with discussion, in the November issue of the ARCHIVES, page 797.

Epidemiology of Inclusion Conjunctivitis (Lantern Demonstration). DR. PHILLIPS THYGESON and DR. WILLIAM STONE JR., New York.

This article will be published in full, with discussion, in a future issue of the ARCHIVES.

Etiology of Uveitis: A Clinical Study of Five Hundred and Sixty-Two Cases (Lantern Demonstration). DR. JACK S. GUYTON and DR. ALLEN C. WOODS, Baltimore.

This article is published in full, with discussion, in this issue of the ARCHIVES, page 983.

Ocular Conditions Associated with Coliform Bacteria: Clinical and Experimental Observations on Coliform Bacteria Infections of the Upper Respiratory Tract (Lantern Demonstration). DR. CONRAD BERENS and DR. EDITH L. NILSON, New York.

This article was published in full, with discussion, in the November issue of the ARCHIVES, page 816.

Tonometric Standardization: A Method of Increasing the Accuracy of Tonometry (Lantern Demonstration). DR. DAVID O. HARRINGTON and DR. ALFRED H. PARSONS, San Francisco.

This article was published in full, with discussion, in the November issue of the ARCHIVES, page 859.

Demonstration Session

Demonstration of Tonometer. DR. DAVID O. HARRINGTON, San Francisco, California.

Corneal Scleral Sutures (Lantern Demonstration). DR. SAMUEL G. HIGGINS, Milwaukee.

This article was published in full in the October issue of the ARCHIVES, page 674.

Hereditary Glaucoma in a Pedigree of Three Generations (Lantern Demonstration). DR. THOMAS D. ALLEN and DR. WALTER G. ACKERMAN, Chicago.

This article will be published in full, with discussion, in a future issue of the ARCHIVES.

Superficial Punctate Parenchymatous Keratitis (Lantern Demonstration). DR. WILLIAM THORNWALL DAVIS, Washington, D. C.

This article will be published in full, with discussion, in a later issue of the ARCHIVES.

Ocular Torticollis: Differential Diagnosis (Lantern Demonstration). DR. LOREN P. GUY, New York.

This article will be published in full, with discussion, in a later issue of the ARCHIVES.

Paralysis of the Superior Rectus and the Inferior Oblique Muscle of the Same Eye (Lantern Demonstration). DR. JAMES W. WHITE, New York.

This article will be published in full, with discussion, in a later issue of the ARCHIVES.

Fusional Movements in Permanent Strabismus: A Study of the Role of the Central and Peripheral Retinal Regions in the Act of Binocular Vision in Squint (Lantern Demonstration). DR. HERMANN M. BURIAN, Hanover, N. H.

This article was published in full, with discussion, in the October issue of the ARCHIVES, page 626.

Directory of Ophthalmologic Societies *

INTERNATIONAL

INTERNATIONAL ASSOCIATION FOR PREVENTION OF BLINDNESS

President: Dr. P. Baillart, 66 Boulevard Saint-Michel, Paris, 6^e, France.
Secretary-General: Prof. M. Van Duyse, Université de Gand, Gand, Prov. Ostflandern, Belgium.
All correspondence should be addressed to the Secretariat, 66 Boulevard Saint-Michel, Paris, 6^e, France.

INTERNATIONAL OPHTHALMOLOGIC CONGRESS

President: Prof. Nordenson, Serafimerlasarettet, Stockholm, Sweden.
Secretary: Dr. Ehlers, Jerbanenegade 41, Copenhagen, Denmark.

INTERNATIONAL ORGANIZATION AGAINST TRACHOMA

President: Dr. A. F. MacCallan, 17 Horseferry Rd., London, England.

PAN-AMERICAN CONGRESS OF OPHTHALMOLOGY

President: Dr. Harry S. Gradle, 58 E. Washington St., Chicago.
Executive Secretaries: Dr. Conrad Berens, 35 E. 70th St., New York. Dr. M. E. Alvaro, 1511 Consolacao, São Paulo, Brazil.

FOREIGN

ALL-INDIA OPHTHALMOLOGICAL SOCIETY

President: Dr. B. K. Narayan Rao, Minto Ophthalmic Hospital, Bangalore.
Secretary: Dr. G. Zachariah, Fritcham, Marshall's Rd., Madras.

BRITISH MEDICAL ASSOCIATION, SECTION ON OPHTHALMOLOGY

President: Dr. W. Clark Souter, 9 Albyn Pl., Aberdeen, Scotland.
Secretary: Dr. Frederick Ridley, 12 Wimpole St., London, W. 1.

CHINESE OPHTHALMOLOGY SOCIETY

President: Dr. C. H. Chou, 363 Avenue Haig, Shanghai.
Secretary: Dr. F. S. Tsang, 221 Foochow Rd., Shanghai.

CHINESE OPHTHALMOLOGICAL SOCIETY OF PEIPING

President: Dr. H. T. Pi, Peiping Union Medical College, Peiping.
Secretary: Dr. C. K. Lin, 180 Hsi-Lo-yen, Chienmeng, Peiping.
Place: Peiping Union Medical College, Peiping. Time: Last Friday of each month.

GERMAN OPHTHALMOLOGICAL SOCIETY

President: Prof. W. Lohlein, Berlin.
Secretary: Prof. E. Engelking, Heidelberg.

HUNGARIAN OPHTHALMOLOGICAL SOCIETY

President: Prof. H. G. Ditroi, Szeged.
Assistant Secretary: Dr. Stephen de Grosz, University Eye Hospital, Maria ucca 39, Budapest.
All correspondence should be addressed to the Assistant Secretary.

MIDLAND OPHTHALMOLOGICAL SOCIETY

President: Dr. W. Niccol, 4 College Green, Gloucester, England.
Secretary: Mr. T. Harrison Butler, 61 Newhall St., Birmingham 3, England.
Place: Birmingham and Midland Eye Hospital.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and keep it up to date.

NORTH OF ENGLAND OPHTHALMOLOGICAL SOCIETY

President: Dr. A. MacRae, 6 Jesmond Rd., Newcastle-upon-Tyne, England.

Secretary: Dr. Percival J. Hay, 350 Glossop Rd., Sheffield 10, England.

Place: Manchester, Bradford, Leeds, Newcastle-upon-Tyne, Liverpool and Sheffield, in rotation. Time: October to April.

OPHTHALMOLOGICAL SOCIETY OF AUSTRALIA

President: Dr. A. James Flynn, 135 Macquarie St., Sydney.

Secretary: Dr. D. Williams, 193 Macquarie St., Sydney.

OPHTHALMOLOGICAL SOCIETY OF EGYPT

President: Prof. Dr. Mohammed Mahfouz Bey, Government Hospital, Alexandria.

Secretary: Dr. Mohammed Khalil, 4 Baehler St., Cairo.

All correspondence should be addressed to the Secretary, Dr. Mohammed Khalil.

OPHTHALMOLOGICAL SOCIETY OF THE UNITED KINGDOM

President: Mr. T. Harrison Butler, 61 Newhall St., Birmingham 3, England.

Secretary: Mr. L. H. Savin, 7 Queen St., London, W. 1, England.

OPHTHALMOLOGY SOCIETY OF BOMBAY

President: Dr. D. D. Sathaye, 127 Girgaum Rd., Bombay 4, India.

Secretary: Dr. H. D. Dastur, Dadar, Bombay 14, India.

Place: H. B. A. Free Ophthalmic Hospital, Parel, Bombay 12. Time: First Friday of every month.

OXFORD OPHTHALMOLOGICAL CONGRESS

Master: Dr. Percival J. Hay, 350 Glossop Rd., Sheffield 10, England.

Secretary-Treasurer: Dr. F. A. Anderson, 12 St. John's Hill, Shrewsbury, England.

PALESTINE OPHTHALMOLOGICAL SOCIETY

President: Dr. Arie Feigenbaum, Abyssinian St. 15, Jerusalem.

Secretary: Dr. E. Sinai, Tel Aviv.

POLISH OPHTHALMOLOGICAL SOCIETY

President: Dr. W. Kapuściński, 2 Waly Batorego, Poznań.

Secretary: Dr. J. Sobański, Lindley'a 4, Warsaw.

Place: Lindley'a 4, Warsaw.

ROYAL SOCIETY OF MEDICINE, SECTION OF OPHTHALMOLOGY

President: Dr. A. J. Ballantyne, 11 Sandyford Pl., Glasgow, C. 3, Scotland.

Secretary: Dr. C. Dee Shapland, 15 Devonshire Pl., London, W. 1, England.

SÃO PAULO SOCIETY OF OPHTHALMOLOGY

President: Dr. Jacques Tupinamba, São Paulo, Brazil.

Secretary: Dr. Silvio de Almeida Toledo, Enfermaria Santa Luzia, Santa Casa de Misericórdia, Cezario Motta St.—112, São Paulo, Brazil.

SOCIEDAD OFTALMOLOGIA DEL LITORAL, ROSARIO (ARGENTINA)

President: Prof. Dr. Carlos Weskamp, Laprida 1159, Rosario.

Secretary: Dr. Juan M. Vila Ortiz, Córdoba 1433, Rosario.

Place: Rosario. Time: Last Saturday of every month, April to November, inclusive.

All correspondence should be addressed to the President.

SOCIEDADE DE OPHTALMOLOGIA E OTO-RHINO-LARYNGOLOGIA DA BAHIA

President: Dr. Francisco Ferreira, Pitangueiras 15, Brotas, S. Salvador, Brazil.

Secretary: Dr. Adroaldo de Alencar, Brazil.

All correspondence should be addressed to the President.

SOCIETÀ OFTALMOLOGICA ITALIANA

President: Prof. Dott. Giuseppe Ovio, Ophthalmological Clinic, University of Rome, Rome.

Secretary: Prof. Dott. Epimaco Leonardi, Via del Gianicolo. 1, Rome.

SOCIÉTÉ FRANÇAISE D'OPHTALMOLOGIE

Secretary: Dr. René Onfray, 6 Avenue de la Motte Picquet, Paris, 7^e.

SOCIETY OF SWEDISH OPHTHALMOLOGISTS

President: Prof. K. G. Ploman, Stockholm.

Secretary: Dr. K. O. Granström, Södermalmstorg 4 Ill tr., Stockholm, Sö.

TEL AVIV OPHTHALMOLOGICAL SOCIETY

President: Dr. D. Arie-Friedman, 96 Allenby St., Tel Aviv, Palestine.

Secretary: Dr. Sadger Max, 9 Bialik St., Tel Aviv, Palestine.

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON OPHTHALMOLOGY

Chairman: Dr. Lawrence T. Post, 508 N. Grand Blvd., St. Louis, Mo.

Secretary: Dr. Derrick Vail, 441 Vine St., Cincinnati.

Place: Atlantic City. Time: June 8-12, 1942.

AMERICAN ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY, SECTION ON OPHTHALMOLOGY

President: Dr. Frank R. Spencer, Physicians' Bldg., Boulder, Colo.

President-Elect: Dr. Ralph I. Lloyd, 14-8th Ave., Brooklyn.

Executive Secretary-Treasurer: Dr. William P. Wherry, 1500 Medical Arts Bldg., Omaha.

Place: Chicago. Time: Oct. 19-24, 1941.

Place: Marinette. Time: November 1941.

Secretary: Dr. G. L. McCormick, 626 S. Central Ave., Marshfield.

AMERICAN OPHTHALMOLOGICAL SOCIETY

President: Dr. Allen Greenwood, 82 Commonwealth Ave., Boston.

Secretary-Treasurer: Dr. Eugene M. Blake, 303 Whitney Ave., New Haven, Conn.

ASSOCIATION FOR RESEARCH IN OPHTHALMOLOGY, INC.

Chairman: Dr. John Evans, 23 Schermerhorn St., Brooklyn.

Secretary-Treasurer: Dr. C. S. O'Brien, University Hospital, Iowa City.

CANADIAN MEDICAL ASSOCIATION, SECTION ON OPHTHALMOLOGY

President: Dr. Alexander E. MacDonald, 170 St. George St., Toronto.

Secretary-Treasurer: Dr. L. J. Sebert, 170 St. George St., Toronto.

CANADIAN OPHTHALMOLOGICAL SOCIETY

President: Dr. J. Vaillancourt, 46 St. Louis St., Quebec.

Secretary-Treasurer: Dr. Alexander E. MacDonald, 421 Medical Arts Bldg., Toronto.

NATIONAL SOCIETY FOR THE PREVENTION OF BLINDNESS

President: Mr. Mason H. Bigelow, 1790 Broadway, New York.

Secretary: Miss Regina E. Schneider, 1790 Broadway, New York.

Executive Director: Mrs. Eleanor Brown Merrill, 1790 Broadway, New York.

SECTIONAL

ACADEMY OF MEDICINE OF NORTHERN NEW JERSEY, SECTION ON EYE, EAR, NOSE AND THROAT

President: Dr. Charles W. Barkhorn, 223 Roseville Ave., Newark.

Secretary: Dr. William F. McKim, 317 Roseville Ave., Newark.

Place: 91 Lincoln Park South, Newark. Time: 8:45 p. m., second Monday of each month, October to May.

CENTRAL WISCONSIN SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. D. G. Hugo, 130 Main St., Oshkosh.

Secretary: Dr. G. L. McCormick, 626 S. Central Ave., Marshfield.

Place: Land O'Lakes. Time: June 1942.

NEW ENGLAND OPHTHALMOLOGICAL SOCIETY

President: Dr. William D. Rowland, 84 Commonwealth Ave., Boston.
 Secretary-Treasurer: Dr. Trygve Gundersen, 243 Charles St., Boston.
 Place: Massachusetts Eye and Ear Infirmary, 243 Charles St., Boston. Time:
 8 p. m., third Tuesday of each month from November to April, inclusive.

PACIFIC COAST OTO-OPHTHALMOLOGICAL SOCIETY

President: Dr. Isaac H. Jones, 635 S. Westlake Ave., Los Angeles.
 Secretary-Treasurer: Dr. C. Allen Dickey, 450 Sutter St., San Francisco.

PUGET SOUND ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Spencer S. Howe, 103 E. Holly St., Bellingham, Wash.
 Secretary-Treasurer: Dr. Barton E. Peden, 419 Stimson Bldg., Seattle.
 Place: Seattle or Tacoma, Wash. Time: Third Tuesday of each month, except
 June, July and August.

ROCK RIVER VALLEY EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. W. H. Elmer, 321 W. State St., Rockford, Ill.
 Secretary-Treasurer: Dr. Harry R. Warner, 321 W. State St., Rockford, Ill.
 Place: Rockford, Ill., or Janesville or Beloit, Wis. Time: Third Tuesday of
 each month from October to April, inclusive.

SAGINAW VALLEY ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. M. Kessler, 311 Center Ave., Bay City, Mich.
 Secretary-Treasurer: Dr. J. H. Curts, 330 S. Washington Ave., Saginaw, Mich.
 Place: Saginaw or Bay City, Mich. Time: Second Tuesday of each month, except
 July and August.

SIoux VALLEY EYE AND EAR ACADEMY

President: Dr. J. C. Davis, 1615 Howard St., Omaha.
 Secretary-Treasurer: Dr. J. E. Dvorak, 408 Davidson Bldg., Sioux Falls, S. D.

SOUTHERN MEDICAL ASSOCIATION, SECTION ON EYE, EAR, NOSE AND THROAT

Chairman: Dr. L. Chester McHenry, Medical Arts Bldg., Oklahoma City.
 Secretary: Dr. J. W. Jervey Jr., 101 Church St., Greenville, S. C.
 Place: Richmond, Va. Time: November 1942.

SOUTHWESTERN ACADEMY OF EYE, EAR, NOSE AND THROAT

President: Dr. Franklin P. Maury, Professional Bldg., Tucson, Ariz.
 Secretary: Dr. A. E. Cruthirds, 1011 Professional Bldg., Phoenix, Ariz.

SOUTHWESTERN MICHIGAN TRIOLOGICAL SOCIETY

President: Dr. W. M. Dodge, 716 First National Bank Bldg., Battle Creek.
 Secretary-Treasurer Dr. Kenneth Lowe, 25 W. Michigan Ave., Battle Creek.
 Time: Last Thursday of September, October, November, March, April and May.

WESTERN PENNSYLVANIA EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. C. H. Bailey, 29 S. Oakland Ave., Sharon.
 Secretary-Treasurer: Dr. J. McClure Tyson, Deposit Nat'l Bank Bldg., DuBois.

STATE

ARKANSAS STATE MEDICAL SOCIETY, EYE, EAR, NOSE AND THROAT SECTION

President: Dr. R. R. Kirkpatrick, 6th and Walnut Sts., Texarkana, Ark.
 Secretary-Treasurer: Dr. Raymond C. Cook, 701 Main St., Little Rock.

COLORADO OPHTHALMOLOGICAL SOCIETY

President: Dr. William M. Bane, 1612 Tremont Pl., Denver.
 Secretary: Dr. Harry Shankel, Republic Bldg., Denver.
 Place: University Club, Denver. Time: 7:30 p. m., third Saturday of each
 month, October to May, inclusive.

CONNECTICUT STATE MEDICAL SOCIETY, SECTION ON EYE, EAR,
NOSE AND THROAT

President: Dr. Edward N. DeWitt, 836 Myrtle Ave., Bridgeport.
Secretary-Treasurer: Dr. Henry L. Birge, 179 Allyn St., Hartford.

EYE, EAR, NOSE AND THROAT CLUB OF GEORGIA

President: Dr. E. N. Maner, 247 Bull St., Savannah.
Secretary-Treasurer: Dr. C. K. McLaughlin, 567 Walnut St., Macon.

INDIANA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. F. McK. Ruby, Union City.
Secretary: Dr. Edwin W. Dyar Jr., 23 E. Ohio St., Indianapolis.
Place: French Lick. Time: First Wednesday in April.

IOWA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. J. K. Von Lackum, 117-3d St. S.E., Cedar Rapids.
Secretary-Treasurer: Dr. B. M. Merkel, 604 Locust St., Des Moines.

LOUISIANA-MISSISSIPPI OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President: Dr. Henry N. Blum, 912 American Bank Bldg., New Orleans.
Secretary-Treasurer: Dr. Edley H. Jones, 1301 Washington St., Vicksburg, Miss.

MICHIGAN STATE MEDICAL SOCIETY, SECTION OF OPHTHALMOLOGY
AND OTOLARYNGOLOGY

Chairman: Dr. Robert H. Fraser, 25 W. Michigan Ave., Battle Creek.
Secretary: Dr. R. G. Laird, 114 Fulton St., Grand Rapids.

MINNESOTA ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. Erling Wilhelm Hansen, 78 S. 9th St., Minneapolis.
Secretary-Treasurer: Dr. George E. McGear, 920 Medical Arts Bldg., Minneapolis.
Time: Second Friday of each month from October to May.

MONTANA ACADEMY OF OTO-OPHTHALMOLOGY

President: Dr. A. L. Hammerel, 208 N. Broadway, Billings.
Secretary: Dr. Fritz D. Hurd, 309 Medical Arts Bldg., Great Falls.

NEBRASKA ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. John Peterson, 1307 N St., Lincoln.

NEW JERSEY STATE MEDICAL SOCIETY, SECTION ON OPHTHALMOLOGY,
OTOLOGY AND RHINOLARYNGOLOGY

Chairman: Dr. Edgar P. Cardwell, 47 Central Ave., Newark.
Secretary: Dr. Arthur E. Sherman, 243 S. Harrison St., East Orange.

NEW YORK STATE MEDICAL SOCIETY, EYE, EAR, NOSE AND THROAT SECTION

Chairman: Dr. Searle B. Marlow, 109 S. Warren St., Syracuse.
Secretary: Dr. C. Stewart Nash, 277 Alexander St., Rochester.

NORTH CAROLINA EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. M. R. Gibson, Professional Bldg., Raleigh.
Secretary: Dr. Vanderbilt F. Couch, 105 W. 4th St., Winston-Salem.

NORTH DAKOTA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. A. E. Spear, Dickinson.
Secretary-Treasurer: Dr. F. L. Wicks, 516-6th St., Valley City.

OREGON ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Paul Bailey, 833 S. W. 11th Ave., Portland.
 Secretary-Treasurer: Dr. R. S. Fixott, 1020 S. W. Taylor St., Portland.
 Place: Good Samaritan Hospital, Portland. Time: Third Tuesday of each month.

RHODE ISLAND OPHTHALMOLOGICAL AND OTOLOGICAL SOCIETY

Acting President: Dr. N. Darrell Harvey, 112 Waterman St., Providence.
 Secretary-Treasurer: Dr. Linley C. Happ, 124 Waterman St., Providence.
 Place: Rhode Island Medical Society Library, Providence. Time: 8:30 p. m.,
 second Thursday in October, December, February and April.

SOUTH CAROLINA SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. J. L. Sanders, 222 N. Main St., Greenville.
 Secretary: Dr. J. H. Stokes, 125 W. Cheves St., Florence.
 Place: Columbia. Time: November 1942.

TENNESSEE ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. Wesley Wilkerson, 700 Church St., Nashville.
 Secretary-Treasurer: Dr. W. D. Stinson, 124 Physicians and Surgeons Bldg.,
 Memphis.

TEXAS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President: Dr. E. L. Goar, 1300 Walker Ave., Houston.
 Secretary: Dr. Dan Brannin, 929 Medical Arts Bldg., Dallas.
 Place: San Antonio. Time: December 1941.

UTAH OPHTHALMOLOGICAL SOCIETY

President: Dr. Everett B. Muir, Boston Bldg., Salt Lake City.
 Secretary-Treasurer: Dr. Earl H. Phillips, 623 Judge Bldg., Salt Lake City.
 Place: University Club, Salt Lake City. Time: 7:00 p. m., third Monday of
 each month.

VIRGINIA SOCIETY OF OTO-LARYNGOLOGY AND OPHTHALMOLOGY

President: Dr. George G. Hawkins, Newport News.
 Secretary-Treasurer: Dr. Guy Fisher, 3 E. Beverley St., Staunton.

WEST VIRGINIA STATE MEDICAL ASSOCIATION, EYE, EAR, NOSE
 AND THROAT SECTION

President: Dr. George Traugh, 309 Cleveland Ave., Fairmont.
 Secretary: Dr. Welch England, 621½ Market St., Parkersburg.

LOCAL

AKRON ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. George E. Black, 7 W. Bowery St., Akron, Ohio.
 Secretary-Treasurer: Dr. C. R. Andersen, 106 S. Main St., Akron, Ohio.
 Time: First Monday in January, March, May and November.

ATLANTA EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. Stacy C. Howell, 144 Ponce de Leon Ave. N. E., Atlanta, Ga.
 Secretary: Dr. Lester A. Brown, 478 Peachtree St. N. E., Atlanta, Ga.
 Place: Grady Hospital. Time: 6:00 p. m., second Wednesday of each month
 from October to May.

BALTIMORE MEDICAL SOCIETY, SECTION ON OPHTHALMOLOGY

Chairman: Dr. Ernst Bodenheimer, 1212 Eutaw Pl., Baltimore.
 Secretary: Dr. Thomas R. O'Rourke, 104 W. Madison St., Baltimore.
 Place: Medical and Chirurgical Faculty, 1211 Cathedral St. Time: 8:30 p. m.
 fourth Thursday of each month from October to March.

BIRMINGHAM EYE, EAR, NOSE AND THROAT CLUB

President: Each member, in alphabetical order.

Secretary: Dr. Luther E. Wilson, 919 Woodward Bldg., Birmingham, Ala.

Place: Tutwiler Hotel. Time: 6:30 p. m., second Tuesday of each month, September to May, inclusive.

BROOKLYN OPHTHALMOLOGICAL SOCIETY

President: Dr. Maurice Wieselthier, 1322 Union St., Brooklyn.

Secretary-Treasurer: Dr. Harold F. Schilback, 142 Joralemon St., Brooklyn.

Place: Kings County Medical Society Bldg., 1313 Bedford Ave. Time: Third Thursday in February, April, May, October and December.

BUFFALO OPHTHALMOLOGIC CLUB

President: Dr. Meyer H. Riwchun, 367 Linwood Ave., Buffalo.

Secretary-Treasurer: Dr. Sheldon B. Freeman, 196 Linwood Ave., Buffalo.

Time: Second Thursday of each month.

CHATTANOOGA SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Each member, in alphabetical order.

Secretary: Dr. Douglas Chamberlain, Chattanooga Bank Bldg., Chattanooga, Tenn.

Place: Mountain City Club. Time: Second Thursday of each month from September to May.

CHICAGO OPHTHALMOLOGICAL SOCIETY

President: Dr. Sanford Gifford, 720 N. Michigan Ave., Chicago.

Secretary-Treasurer: Dr. Vernon M. Leech, 55 E. Washington St., Chicago.

Place: Chicago Towers Club, 505 N. Michigan Ave. Time: Third Monday of each month from October to May.

CINCINNATI GENERAL HOSPITAL OPHTHALMOLOGY STAFF

Chairman: Dr. D. T. Vail, 441 Vine St., Cincinnati.

Secretary: Dr. A. A. Levin, 441 Vine St., Cincinnati.

Place: Cincinnati General Hospital. Time: 7:45 p. m., third Friday of each month except June, July and August.

CLEVELAND OPHTHALMOLOGICAL CLUB

Chairman: Dr. W. J. Abbott, 10515 Carnegie Ave., Cleveland.

Secretary: Dr. L. V. Johnson, 2065 Adelbert Rd., Cleveland.

Time: Second Tuesday in October, December, February and April.

COLLEGE OF PHYSICIANS, PHILADELPHIA, SECTION ON OPHTHALMOLOGY

Chairman: Dr. Francis H. Adler, 313 S. 17th St., Philadelphia.

Clerk: Dr. W. S. Reese, 1901 Walnut St., Philadelphia.

Time: Third Thursday of every month from October to April, inclusive.

COLUMBUS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

Chairman: Dr. C. D. Postle, 240 E. State St., Columbus, Ohio.

Secretary-Treasurer: Dr. Hugh C. Thompson, 289 E. State St., Columbus, Ohio.

Place: The Neil House. Time: 6 p. m., first Monday of each month.

CORPUS CHRISTI EYE, EAR, NOSE AND THROAT SOCIETY

Chairman: Dr. F. K. Stroud, 416 Chaparral St., Corpus Christi, Texas.

Secretary: Dr. Arthur Padilla, 414 Medical Professional Bldg., Corpus Christi, Texas.

Time: Second Friday of each month from October to May.

DALLAS ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. L. A. Nelson, 4105 Live Oak St., Dallas, Texas.
 Secretary: Dr. S. F. Harrington, 921 Medical Arts Bldg., Dallas, Texas.
 Place: Dallas Athletic Club. Time: 6:30 p. m., first Tuesday of each month from October to June. The November, January and March meetings are devoted to clinical work.

DES MOINES ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. H. C. Schmitz, 604 Locust St., Des Moines, Iowa.
 Secretary-Treasurer: Dr. Byron M. Merkel, 604 Locust St., Des Moines, Iowa.
 Time: 7:45 p. m., third Monday of every month from September to May.

DETROIT OPHTHALMOLOGICAL CLUB

Chairman: Members rotate alphabetically.
 Secretary: Dr. Harvey E. Dowling, 2414 Eaton Tower, Detroit.
 Time: 6:30 p. m., first Wednesday of each month.

DETROIT OPHTHALMOLOGICAL SOCIETY

President: Dr. Parker Heath, 1553 Woodward Ave., Detroit.
 Secretary: Dr. Leland F. Carter, 1553 Woodward Ave., Detroit.
 Place: Club rooms of Wayne County Medical Society. Time: Third Thursday of each month from November to April, inclusive.

EASTERN NEW YORK EYE, EAR, NOSE AND THROAT ASSOCIATION

President: Dr. James M. Dunn, 1352 Union St., Schenectady.
 Secretary-Treasurer: Dr. Joseph L. Holohan, 330 State St., Albany.
 Time: Third Wednesday in October, November, March, April, May and June.

FORT WORTH EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. W. R. Thompson, 602 W. 10th St., Fort Worth, Texas.
 Secretary-Treasurer: Dr. A. E. Jackson, 602 W. 10th St., Fort Worth, Texas.
 Place: Medical Hall, Medical Arts Bldg. Time: 7:30 p. m., first Friday of each month except July and August.

HOUSTON ACADEMY OF MEDICINE, OPHTHALMOLOGICAL AND
 OTO-LARYNGOLOGICAL SECTION

President: Dr. Wallace W. Ralston, 1304 Walker Ave., Houston, Texas.
 Secretary: Dr. William J. Snow, 708 Medical Arts Bldg., Houston, Texas.
 Place: Medical Arts Bldg., Harris County Medical Society Rooms. Time: 8 p. m., second Thursday of each month from September to June.

INDIANAPOLIS OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President: Dr. John I. Garret, 57 Stokes Bldg., Indianapolis.
 Secretary: Dr. Kenneth L. Craft, 23 E. Ohio St., Indianapolis.
 Place: Indianapolis Athletic Club. Time: 6:30 p. m., second Thursday of each month from November to May.

KANSAS CITY SOCIETY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Homer Beal, 1103 Grand Ave., Kansas City, Mo.
 Secretary: Dr. Desmond Curran, Federal Reserve Bank Bldg., Kansas City, Mo.
 Time: Third Thursday of each month from October to June. The November, January and March meetings are devoted to clinical work.

LONG BEACH EYE, EAR, NOSE AND THROAT SOCIETY

Chairman: Dr. Harold Snow, 614 S. Pacific Ave., San Pedro, Calif.
 Secretary-Treasurer: Dr. Oliver R. Nees, 508 Times Bldg., Long Beach, Calif.
 Place: Professional Bldg. Time: Last Wednesday of each month from October to May.

LOS ANGELES SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. Harold Mulligan, 1680 N. Vine St., Los Angeles.

Secretary-Treasurer: Dr. Colby Hall, 1136 W. 6th St., Los Angeles.

Place: Los Angeles County Medical Association Bldg., 1925 Wilshire Blvd. Time: 6:00 p. m., fourth Monday of each month from September to May, inclusive.

LOUISVILLE EYE AND EAR SOCIETY

President: Dr. Joseph S. Heitger, Heyburn Bldg., Louisville, Ky.

Secretary-Treasurer: Dr. J. W. Fish, 321 W. Broadway, Louisville, Ky.

Place: Brown Hotel. Time: 6:30 p. m., second Thursday of each month from September to May, inclusive.

MEDICAL SOCIETY OF THE DISTRICT OF COLUMBIA, SECTION OF
OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman: Dr. E. J. Cummings, 1835 I St. N. W., Washington.

Secretary: Dr. P. S. Constantinople, 1835 I St. N. W., Washington.

Place: 1718 M St. N. W. Time: 8 p. m., third Friday of each month from October to April, inclusive.

MEMPHIS SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman: Each member, in alphabetical order.

Secretary: Dr. Sam H. Sanders, 1089 Madison Ave., Memphis, Tenn.

Place: Eye Clinic of Memphis Eye, Ear, Nose and Throat Hospital. Time: 8 p. m., second Tuesday of each month from September to May.

MILWAUKEE OTO-OPHTHALMIC SOCIETY

President: Dr. John B. Hitz, 411 E. Mason St., Milwaukee.

Secretary-Treasurer: Dr. Ralph T. Rank, 238 W. Wisconsin Ave., Milwaukee.

Place: University Club. Time: 6:30 p. m., second Tuesday of each month.

MONTGOMERY COUNTY MEDICAL SOCIETY

Chairman: Dr. H. V. Dutrow, 1040 Fidelity Medical Bldg., Dayton, Ohio.

Secretary-Treasurer: Dr. Maitland D. Place, 981 Reibold Bldg., Dayton, Ohio.

Place: Van Cleve Hotel. Time: 6:30 p. m., first Tuesday of each month from October to June, inclusive.

MONTREAL OPHTHALMOLOGICAL SOCIETY

President: Dr. J. Rosenbaum, 1396 Ste. Catherine St. W., Montreal, Canada.

Secretary: Dr. L. Tessier, 1230 St. Joseph Blvd. E., Montreal, Canada.

Time: Second Thursday of October, December, February and April.

NASHVILLE ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman: Dr. Andrew Hollabaugh, Doctors Bldg., Nashville, Tenn.

Secretary: Dr. Guy Maness, Medical Arts Bldg., Nashville, Tenn.

Place: St. Thomas Hospital. Time: 8 p. m., third Monday of each month from October to May.

NEW HAVEN OPHTHALMOLOGICAL SOCIETY

President: Dr. William H. Ryder, 185 Church St., New Haven, Conn.

Secretary: Dr. Frederick A. Wies, 255 Bradley St., New Haven, Conn.

NEW ORLEANS OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President: Dr. W. B. Clark, 1012 American Bank Bldg., New Orleans.

Secretary: Dr. Mercer G. Lynch, 1018 Maison Blanche Bldg., New Orleans.

Place: Louisiana State University Medical Bldg. Time: 8 p. m., second Tuesday of each month from October to May.

NEW YORK ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

Chairman: Dr. Kaufman Schlivek, 1016-5th Ave., New York.

Secretary: Dr. Brittain Payne, 896 Madison Ave., New York.

Time: 8:30 p. m., third Monday of every month from October to May, inclusive.

NEW YORK SOCIETY FOR CLINICAL OPHTHALMOLOGY

President: Dr. James W. Smith, 1016-5th Ave., New York.
 Secretary: Dr. Benjamin Esterman, 983 Park Ave., New York.
 Place: Squibb Hall, 745-5th Ave. Time: 8 p. m., first Monday of each month from October to May, inclusive.

OKLAHOMA CITY ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. R. E. Leatherock, Cushing, Okla.
 Secretary: Dr. Harry C. Ford, 1014 Medical Arts Bldg., Oklahoma City.
 Place: University Hospital. Time: Second Tuesday of each month from September to May.

OMAHA AND COUNCIL BLUFFS OPHTHALMOLOGICAL AND
 OTO-LARYNGOLOGICAL SOCIETY

President: Dr. Harold Gifford, 1620 Medical Arts Bldg., Omaha.
 Secretary-Treasurer: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha.
 Place: Omaha Club, 20th and Douglas Sts., Omaha. Time: 6 p. m., dinner; 7 p. m., program; third Wednesday of each month from October to May.

PASSAIC-BERGEN OPHTHALMOLOGICAL CLUB

President: Dr. L. Markowitz, 16 Church St., Paterson, N. J.
 Secretary-Treasurer: Dr. A. John Reinhorn, 302 Broadway, Paterson, N. J.
 Place: Paterson Eye and Ear Infirmary. Time: 9 p. m., last Friday of every month, except June, July and August.

PHILADELPHIA COUNTY MEDICAL SOCIETY, EYE SECTION

Chairman: Dr. Edmund B. Spaeth, 1930 Chestnut St., Philadelphia.
 Secretary: Dr. Wilfred E. Fry, 1819 Chestnut St., Philadelphia.
 Time: First Thursday of each month from October to May.

PITTSBURGH OPHTHALMOLOGICAL SOCIETY

President: Dr. J. Clyde Markel, 200-9th St., Pittsburgh.
 Secretary: Dr. George H. Shuman, 351-5th Ave., Pittsburgh.
 Place: Pittsburgh Academy of Medicine Bldg. Time: Fourth Monday of each month, except June, July, August and September.

READING EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. James E. Landis, 232 N. 6th St., Reading, Pa.
 Secretary: Dr. Paul C. Craig, 232 N. 5th St., Reading, Pa.
 Place: Wyomissing Club. Time: 6:30 p. m., third Wednesday of each month from October to July.

RICHMOND OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President: Dr. W. F. Bryce, Medical Arts Bldg., Richmond, Va.
 Secretary: Dr. Richard W. Vaughan, Medical Arts Bldg., Richmond, Va.
 Place: Westmoreland Club. Time: 6 p. m., second Monday of each month from October to May.

ROCHESTER EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. E. J. Avery, 11 N. Goodman St., Rochester, N. Y.
 Secretary-Treasurer: Dr. Charles T. Sullivan, 277 Alexander St., Rochester, N. Y.

ST. LOUIS OPHTHALMIC SOCIETY

President: Dr. William M. James, 508 N. Grand Blvd., St. Louis.
 Secretary: Dr. H. Rommel Hildreth, 823 Metropolitan Bldg., St. Louis.
 Place: Oscar Johnson Institute. Time: Clinical meeting 5:30 p. m., dinner and scientific meeting 6:30 p. m., fourth Friday of each month from October to April, inclusive, except December.

SAN ANTONIO OPHTHALMOLO-OTO-LARYNGOLOGICAL SOCIETY

President: Dr. Dan Russell, 705 E. Houston St., San Antonio, Texas.
 Secretary-Treasurer: Dr. P. G. Bowen, 315 Camden St., San Antonio, Texas.
 Place: Bexar County Medical Library. Time: 8 p. m., first Tuesday of each month from October to May.

SAN FRANCISCO COUNTY MEDICAL SOCIETY, SECTION ON EYE,
EAR, NOSE AND THROAT

Chairman: Dr. Fred Boyle, 490 Post St., San Francisco.
 Secretary: Dr. Frank Hand, 450 Sutter St., San Francisco.
 Place: Society's Bldg., 2180 Washington St., San Francisco. Time: Fourth Tuesday of every month except June, July and December.

SHREVEPORT EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. David C. Swearingen, Slattery Bldg., Shreveport, La.
 Secretary-Treasurer: Dr. Kenneth Jones, Medical Arts Bldg., Shreveport, La.
 Place: Shreveport Charity Hospital. Time: 7:30 p. m., first Monday of every month except July, August and September.

SPOKANE ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Louis A. Parsell, 407 Riverside Ave., Spokane, Wash.
 Secretary: Dr. Robert L. Pohl, 407 Riverside Ave., Spokane, Wash.
 Place: Paulsen Medical and Dental Library. Time: 8 p. m., fourth Tuesday of each month except June, July and August.

SYRACUSE EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. Roy Seeley Moore, 1704 State Tower Bldg., Syracuse, N. Y.
 Secretary-Treasurer: Dr. I. H. Blaisdell, 713 E. Genesee St., Syracuse, N. Y.
 Place: University Club. Time: First Tuesday of each month except June, July and August.

TOLEDO EYE, EAR, NOSE AND THROAT SOCIETY

Chairman: Dr. J. E. Minns, 316 Michigan St., Toledo, Ohio.
 Secretary: Dr. John D. Skow, 2001 Collingwood Blvd., Toledo, Ohio.
 Place: Toledo Club. Time: Each month except June, July and August.

TORONTO ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

Chairman: Dr. W. R. F. Luke, 316 Medical Arts Bldg., Toronto, Canada.
 Secretary: Dr. W. T. Gratton, 216 Medical Arts Bldg., Toronto, Canada.
 Place: Academy of Medicine, 13 Queens Park. Time: First Monday of each month, November to April.

WASHINGTON, D. C., OPHTHALMOLOGICAL SOCIETY

President: Dr. E. Leonard Goodman, 1801 I St. N. W., Washington, D. C.
 Secretary-Treasurer: Dr. Sterling Bockoven, 1752 Massachusetts Ave. N. W., Washington, D. C.
 Place: Episcopal Eye, Ear and Throat Hospital. Time: 7:30 p. m., first Monday in November, January, March and April.

WILKES-BARRE OPHTHALMOLOGICAL SOCIETY

Chairman: Each member in turn.
 Secretary: Dr. Samuel T. Buckman, 70 S. Franklin St., Wilkes-Barre, Pa.
 Place: Office of chairman. Time: Last Tuesday of each month from October to May.

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